ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 vs 2 µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

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DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled **"ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 vs 2 µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION"** submitted towards partial fulfillment of the requirements for the award of **MD ANAESTHESIOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Suneet Kant Kathuria,** Professor & Head, Department of Anaesthesiology, **Dr. Neeru Luthra**, Professor, Department of Anaesthesiology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my family

&

Teachers

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COMMIT TO THE LORD WHATEVER YOU DO, AND HE WILL ESTABLISH YOUR PLANS. Successful completion of a task is often less due to individual talent than to the fact that the person has been blessed by the 'GOD ALMIGHTY'.

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Dr. Ashima Mahajan

LIST OF ABBREVIATIONS

%	Percentage
α2-AR	Alpha-2 adrenergic receptor
ASA	American Society of Anesthesiologists
CABG	Coronary artery bypass graft
cm	Centimeter
DBP	Diastolic Blood Pressure
ECG	Electrocardiography
ETT	Endotracheal Tube
HDSR	Haemodynamic stress response
hr	Hour
HR	Heart Rate
HTN	Hypertension
kg	Kilograms
MAP	Mean Arterial Pressure
m	Meter
mg	Milligram
$MgSO_4$	Magnesium sulphate
min	Minutes
ml	Millilitres
mmHg	Millimeters of mercury
NaCl	Sodium Chloride
N_2O	Nitrous Oxide
OR	Operating room
SD	Standard Deviation
SpO_2	Oxygen Saturation
SBP	Systolic Blood Pressure
T2DM	Type2 diabetes mellitus
µg	Microgram

ABSTRACT

Introduction: Laryngoscopy and tracheal intubation are painful stimuli which incite intense sympathetic activity and may be associated with transient but significant haemodynamic changes. Dexmedetomidine is a highly selective alpha-2 adrenergic receptor (α2- AR) agonist has been used for blunting this pressor response. There are conflicting results in various studies on haemodynamic response with nebulisation with various dosages of dexmedetomidine.

Aim of study: We aimed to study the role of pre-operative nebulisation with 1 vs 2µg/kg dexmedetomidine in blunting haemodynamic response to laryngoscopy and intubation.

Materials and methods: A prospective randomized study was conducted on 165 ASA grade I and II adult patients, posted for elective surgery under general anesthesia. Patients were enrolled and randomly allocated into three groups of 55 patients each (Group 0, Group I and Group II) based on computer generated random numbers. Patients in “Group 0” received nebulisation with 5 ml of solution containing 0.9% Sodium chloride (NaCl). Group I and Group II received nebulisation with 5 ml of 0.9% NaCl solution containing 1µg/kg and 2µg/kg dexmedetomidine, respectively, ten-minutes prior to induction of anaesthesia with endotracheal (ET) intubation. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO_2) were recorded by an anaesthesiologist blinded for study, at different time points and compared among the three groups.

Results: Both 1µg/kg and 2µg/kg nebulised dexmedetomidine helps in blunting HR, DBP, SBP and MAP response to laryngoscopy and intubation. However, 2µg/kg dexmedetomidine nebulisation lead to a better control of SBP and MAP than 1µg/kg dexmedetomidine nebulisation. The requirement of induction dose of propofol was lesser in group II compared to group 0 and group 1.

Conclusion: Although pre-operative nebulisation with both 1µg/kg and 2µg/kg dexmedetomidine helps to blunt haemodynamic response to laryngoscopy and intubation, nebulisation with 2µg/kg dexmedetomidine appears to be more effective than nebulisation with 1µg/kg dexmedetomidine in terms of better control of the blood pressure pressor response.

Keywords: Dexmedetomidine, Haemodynamic, Intubation, Laryngoscopy, pressor response, nebulisation.

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INTRODUCTION

Laryngoscopy and tracheal intubation are painful stimuli which incite intense sympathetic activity and are associated with transient but significant haemodynamic changes. This pressor/ haemodynamic response occurs within 30 seconds after laryngoscopy and intubation and lasts for less than ten minutes.[1] It is characterized by hypertension, tachycardia, increased intracranial and intraocular pressures. These transitory responses usually have no consequences in healthy individuals but may be harmful to the patients having reactive airway, hypertension, coronary artery disease, myocardial insufficiency, and cerebrovascular diseases. It can lead to left ventricular failure, myocardial ischemia, ventricular arrhythmias, and cerebrovascular stroke. [2-5]

Manipulation of the airway during laryngoscopy and endotracheal intubation causes stimulation of pharyngeal and tracheolaryngeal nociceptors, which result in haemodynamic stress response (HDSR).[6] These haemodynamic changes are associated with the release of catecholamines. Laryngoscopy alone can also generate essentially the same pressor response as done by laryngoscopy and intubation. These responses are thought to be a somato-visceral reflex in nature.[7]

Stress response is regulated by two primary neuroendocrine systems- the hypothalamus pituitary adrenocortical (HPA) and sympathetic adrenomedullary (SAM) system.[8] Common factors precipitating the pressor response to laryngoscopy and intubation are light planes of anaesthesia, stimulation of vagally innervated posterior part of epiglottis by straight/Miller blade, anatomically difficult view, greater force used to displace the tongue and more manipulations/attempts at laryngoscopy and intubation leading to prolonged time for laryngoscopy and intubation.[9]

In order to keep patient in optimal condition during induction of anaesthesia, it is important to blunt haemodynamic response to laryngoscopy and intubation. Attenuation of this response is a major challenge for an anaesthesiologist.

Different intubating skills and methods such as fiberoptic intubation, deepening of anaesthesia, use of topical anaesthesia and laryngeal mask airway (LMA) can reduce haemodynamic changes. Numerous drugs through different routes have been tried to attenuate the stress response to laryngoscopy and intubation such as - opioids, beta- blockers, calcium channel antagonists, benzodiazepines and dexmedetomidine but each of them has their own advantages and limitations. [1,4,10,11] The method or drug of choice depends on many factors, including the urgency of surgery, choice of anaesthetic technique, route of administration and medical condition of the patient.

Propofol and opioids even though causing sedation and attenuation of haemodynamic response, can lead to respiratory depression. Propofol is an ultra-short-acting intravenous (IV) induction agent with some favorable properties like smooth induction, quick recovery, and antiemetic properties. However, it decreases blood pressure, cardiac output, and systemic vascular resistance due to inhibition of sympathetic vasoconstriction and impairment of baroreceptor reflex regulatory system. These haemodynamic side effects may be exaggerated in hypovolemic and elderly patients with compromised left ventricular function due to coronary artery disease. Fentanyl is a short acting synthetic opioids agonist, 75-125 times more potent than morphine. Fentanyl attenuates haemodynamic stress response by its action on opioid receptors and by decreasing sympathetic outflow. Fentanyl at low dose shows an inconsistent response to laryngoscopy and intubation. High dose however is associated with the risk of respiratory depression and the need for postoperative elective ventilation.[12]

Alpha-2 adrenergic receptor (α2-AR) agonists like clonidine and dexmedetomidine are being increasingly used for blunting sympathoadrenal stimulation caused by tracheal intubation and surgery. α2-AR agonists produce clinical effects after binding to G-Protein-coupled α2-AR. α2-AR are of three subtypes [α2A, α2B, and α2C] with each having different physiological functions and pharmacological activities.[13]

In the heart, the dominant action of α2-AR agonists is a decrease in heart rate through cardio accelerator blockage nerve and bradycardia via α2A-AR through vagomimetic action. Locus coeruleus of brain stem and spinal cord are the principal sites for sedative and analgesic action, respectively, both acting through α2A-AR.[13] Activation of α2-AR leads to dose dependent reduction in level of plasma catecholamines (maximum 89%), bradycardia and hypotension secondary to sympathetic inhibition of medullary vasomotor center.

In addition, clonidine increases the cardiac baroreceptor reflex sensitivity to an increase in the systolic blood pressure, and hence stabilizes the blood pressure. However, its mild selectivity to α2-AR and long half-life has limited its use. Compared to clonidine, dexmedetomidine a newer imidazole derivative, is highly potent, highly selective α2-AR agonist. It causes conscious sedation and analgesia without causing respiratory depression. It has anxiolytic, anti-sialagogue, sympatholytic, cardiovascular, and neurological stabilizing effects. It causes reduction in delirium and agitation. [5,13] Its sedative effect can be reversed by a drug known as atipamezole, which acts by increasing the central turnover of noradrenaline.[5]

Dexmedetomidine functions by stimulating pre and post synaptic α2-AR within the central nervous system, leading to hyperpolarization of noradrenergic neurons, induction of an inhibitory feedback loop and reduction in norepinephrine. This has sympatholytic effect and attenuates the stress responses to noxious stimulus like laryngoscopy and

intubation.[14] Dexmedetomidine in various doses and routes, such as intravenous (IV), intranasal, intramuscular, and nebulised, has been studied to reduce haemodynamic response to intubation.[2]

Dexmedetomidine at an IV loading dose of 0.5 and 1μg/kg, attenuates increase in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) [7] but IV bolus dose may lead to profound bradycardia and hypotension in cardio-compromised and hypovolemic patients.[1]

Intranasal administration of dexmedetomidine (1μg/kg) can also effectively alleviate stress response to tracheal intubation.[15] This route has more gradual onset as compared to the IV route. Through intranasal route, it can penetrate the blood-brain barrier and reach the central nervous system directly. Nasal mucosa has high vascularity, due to which dexmedetomidine can access the systemic circulation rapidly, bypassing the first-pass metabolism of liver.

The intra-nasal method of drug delivery is linked to brief nose discomfort, occasionally coughing, vocal cord irritation or laryngospasm.[1] Nebulising the medication as an atomized spray offered a superior solution to this drawback. Nebulised dexmedetomidine is preferred over both IV and intranasal modes of administration since drug deposition after nebulisation occurs over nasal, buccal, and respiratory mucosa (maximal surface area coverage with a thin coating of medication). Dexmedetomidine bioavailability through buccal and nasal mucosa is 82% and 65%, respectively. [16,17] Also, it avoids transient cough, nasal irritation, and vocal cord irritation. [18] Nebulisation therapy has better patient compliance and most importantly little risk of adverse events compared with other routes of drug administration.

In a study done by Misra et al. [10] nebulisation with 1μg/kg of dexmedetomidine was used for prevention of pressor response and was found to effectively blunt increase in HR, but not SBP following laryngoscopy and intubation. There was a considerable reduction in the dose of propofol required at induction of general anaesthesia in the treatment group. It was found that intraoperative requirement of fentanyl and isoflurane also decreased significantly in the patients nebulised with dexmedetomidine group.

Kumar et al. [1] conducted a study on evaluation of nebulised dexmedetomidine(1μg/kg) in blunting haemodynamic response to intubation. In contrast to study done by Misra et al. it was found that SBP, DBP, and MAP significantly decreased after laryngoscopy and intubation and there was no significant difference in the HR.

Similar study was conducted by Shrivastava P et al. [2] There was significant attenuation of HR, SBP, DBP, and MAP at one minute, five minutes, and ten minutes following intubation in the group of patients who received dexmedetomidine nebulisation (1μg/kg) without any adverse effect.

Due to conflicting results in previous studies on haemodyamic response with nebulisation with 1μg/kg of dexmedetomidine, we plan to compare pre-operative nebulisation with 1μg/kg and 2μg/kg of dexmedetomidine to find an optimal dose for blunting haemodynamic response to laryngoscopy and intubation with minimal side effects.

AIMS AND OBJECTIVES

Primary aim:

- Role of pre-operative dexmedetomidine nebulisation with 1 vs 2μg/kg in blunting haemodynamic response to laryngoscopy and intubation.

Secondary aim:

- To compare dose sparing effect of 1 and 2μg/kg dexmedetomidine nebulisation on propofol induction dose.
- To study adverse effects associated with 1 and 2μg/kg of dexmedetomidine nebulisation.

REVIEW OF LITERATURE

Laryngoscopy and intubation of the trachea are painful stimuli which leads to sympathetic haemodynamic stress response (HDSR) that occurs as increase in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR). [19,20] These painful stimuli are initiated by proprioceptors in response to tissue irritation in the supraglottic region and trachea. Impulses from these receptors are transmitted by glossopharyngeal and vagus nerves to the brainstem which leads to increased hypothalamic-pituitary activity further resulting into increase in circulating plasma catecholamines.[21] This HDSR to intubation is generally of brief duration and of little clinical significance in healthy individuals. It is deleterious to those with systemic hypertension, coronary heart diseases, valvular cardiac diseases, and the complications like myocardial ischemia, left ventricular failure, cerebral haemorrhage and cardiac dysrhythmias can occur. [20-23]

Many drugs have been used for blunting cardiovascular responses to laryngoscopy and intubation including lignocaine (intravenous and topical), magnesium sulphate ($MgSO_4$), opioids, antihypertensive agents (like phentolamine, sodium nitroprusside, beta blockers, nitroglycerine, calcium channel blockers, etc.) and dexmedetomidine [1,4,10,11]

Clonidine and dexmedetomidine are alpha-2 adrenergic receptor (α2-AR) agonists being increasingly used for blunting sympathoadrenal stimulation caused by tracheal intubation and surgery. Dexmedetomidine is a specific and selective α2-AR agonist as compared to clonidine. It has shorter duration of action and has sympatholytic, sedative, amnesic and analgesic properties. It stimulates α2-AR in lateral reticular nucleus resulting in reduced central sympathetic outflow and blunting of haemodynamic responses to unpleasant stimulation and hence preventing the overall haemodynamic variability. [24,25] It produces co-operative or arousable

sedation, which is different from clouding of consciousness induced by drugs acting on GABA system.

Dexmedetomidine has been used in various doses and routes like intravenously, intranasally, intramuscularly and nebulised for its ability to lessen the hemodynamic response to laryngoscopy and intubation.

Dexmedetomidine as an intravenous (IV) bolus dose causes profound bradycardia and hypotension. Advantage of nebulised dexmedetomidine over intranasal is that, it avoids transient cough, nasal irritation, vocal cord irritation or laryngospasm.[18] Nebulised dexmedetomidine may be a superior option than both intravenous and intranasal modes of administration since drug deposition after nebulisation occurs over nasal, buccal, and respiratory mucosa. Bioavailability of nebulised dexmedetomidine is 82% through buccal mucosa and 65% through nasal mucosa. [16,17]

Lawrence, et al. [26] researched the effects of a single preoperative dosage of 2 μg/kg dexmedetomidine given intravenously, on the need for isoflurane and peri-operative hemodynamic stability. According to their study, dexmedetomidine administration decreased both the intraoperative heart rate variability and the haemodynamic response to tracheal intubation and extubation. Dexmedetomidine administration also resulted in decreased postoperative analgesic and antiemetic requirement as well as perioperative serum catecholamine concentrations. However, hypotension and bradycardia occurred more frequently after the use of dexmedetomidine.

Munise Yildiz et al. [27] (2006) conducted a study on 50 patients divided into 2 group (dexmedetomidine group and placebo group, n = 25 in each group), for studying effect of dexmedetomidine on haemodynamic

responses to laryngoscopy and intubation. It was concluded that pre-operative single dose (1µg/kg) of IV dexmedetomidine resulted in deep sedation, reduced opioid and anaesthetic requirements and blunted the haemodynamic responses following laryngoscopy. Moreover, dexmedetomidine decreased blood pressure and HR as well as the recovery time after the operation.

A study was conducted by Silpa et al. [28] in which they compared the efficacy of dexmedetomidine given preoperatively at two different doses as IV infusions over 15 minutes (min) in attenuating the hemodynamic response to endotracheal intubation in 70 patients undergoing elective cardiac surgeries. They concluded that Dexmedetomidine in a dose of 0.5 µg/kg is less effective than 1 µg/kg for attenuation of hemodynamic stress response to intubation in cardiac surgery. A more graded increase in the dose of dexmedetomidine may lead to an optimum dose in attenuating the hemodynamic response to intubation. Administration of 1 µg/kg dexmedetomidine was not accompanied by bradycardia. Hypotension occurred in one patient in each group.

Md Shabaz Alam et al. [3] (2017) conducted a study on 100 patients divided into 2 groups and compared the effects of IV dexmedetomidine (1.0 µg/kg as slow IV infusion over a period of ten min, ten min before induction of anaesthesia) and IV $MgSO_4$ (60 mg/kg of 50% $MgSO_4$, ten min before induction of anaesthesia) on haemodynamic parameters in patients undergoing laryngoscopy and intubation. It was concluded that both drugs lead to haemodynamic stability but, dexmedetomidine was more effective in controlling the HR.

Mahajan, et al. [29] conducted study on 130 patients of ASA I and II scheduled for elective surgery under general anaesthesia. Patients were randomized to receive either dexmedetomidine 1 µg/kg (Group DS),

$MgSO_4$ 30 mg/kg (Group MS) diluted in 100 ml saline or 100 ml normal saline (Group NS) 15 min before induction of anaesthesia. The effects of IV dexmedetomidine vs $MgSO_4$ on the pressor responses to laryngoscopy and endotracheal intubation was investigated. Both the dexmedetomidine and $MgSO_4$ groups had considerably reduced HR and BP (P 0.001), but dexmedetomidine was responsible for much lower values in comparison due to its sympatholytic and vagomimetic effects. MgSO4 turned out to be a more effective medication than dexmedetomidine. Therefore, their study suggested that even though, intravenous dexmedetomidine was able to obtund the haemodynamic response to laryngoscopy, it did not help in maintaining the haemodynamic stability.

Neha Sharma et al. [30] (2018) conducted a study on 90 ASA I and II, age 16-65 years patients for studying therapeutic efficacy of two different doses of dexmedetomidine on haemodynamic response to intubation and effect on induction dose of propofol. Patients were divided into three groups. Group I and Group II received 0.5μg/kg and 1μg/kg IV dexmedetomidine, respectively, in ten ml saline over ten min intravenously and Group III is control group, received normal saline 10 ml bolus intravenously, before induction. This study concluded that the haemodynamic response was sufficiently blunted with both the doses of dexmedetomidine. Hypotension was seen in one patient in Group I compared to none of the patients in the other two groups. Bradycardia was seen in 2 patients in Group I and 1 patient in Group II and none in Group III. Thus, lower dose (0.5μg/kg) besides being cost-effective, was associated with lesser incidence of adverse effects such as hypotension and bradycardia as compared to high dose (1μg/kg). Both doses of 0.5μg/kg and 1μg/kg were equally effective in decreasing the requirement of induction dose of propofol

Danilo Nava et al.[7] (2018) conducted a study on 60 patients for evaluation of effect of IV dexmedetomidine on suppression of adrenergic response to laryngoscopy and intubation.1st group received dexmedetomidine dose of 0.5μg/kg and 2nd group received dose of 1μg/kg of same drug which was administered over ten min, ten min before induction of anaesthesia. It was concluded that dexmedetomidine 0.5 μg/kg intravenously was associated with greater than 20% increase in SBP, DBP, MAP and HR after endotracheal intubation and was not sufficient for hemodynamic stability. Intravenous dose of dexmedetomidine 1μg/kg causes significant decrease in increased heart rate, SBP, DBP and MAP upto 3 min post-intubation.

A study was conducted by Eman Ahmed Ismail et al. [31] on 70 ASA II patients with age ranges from 20 to 60 years to assess the effects of single dose of dexmedetomidine on haemodynamic response to tracheal intubation in controlled hypertensive patients. Seventy patients divided into two equal groups; group A received IV dexmedetomidine 0.5 μg/kg diluted to 20 ml with 0.9% sodium chloride (NaCl) and group B received 20 ml of 0.9% NaCl. It was concluded that dexmedetomidine 0.5 μg/kg over ten-min infusion prior to induction of anesthesia significantly blunted the hemodynamic response to laryngoscopy and intubation in controlled hypertensive patients. No side effects were recorded in both studied groups such as bradycardia and hypotension. None of the patients needed drug intervention.

Xiaoxia Gu et al.[15] conducted a study on effect of intranasal dexmedetomidine as premedication on sedation and stress of tracheal intubation undergoing gynaecological laparoscopic surgery on 40 ASA I-II patients aged 20-50 years. Group D received 1ug/kg dexmedetomidine by intranasal route and Group C (control) received same volume of normal saline by intranasal route, 30 min before induction of anaesthesia. It was

seen that the concentrations of catecholamines in the control group increased significantly, while the concentrations of catecholamines in group D also increased, but were still lower than the baseline values, with no statistical significance (P>0.05). It was concluded that intranasal administration of dexmedetomidine (1μg/kg) had a better control of HR, SBP, DBP in response to tracheal intubation whereas, the control group did not inhibit the stress response of endotracheal intubation satisfactorily.

In a study conducted by Salkat Niyogi et al. [5] on 70 adult's patients, IV and intranasal route of dexmedetomidine was compared for attenuation of haemodynamic response to laryngoscopy and intubation. Patients were divided into two group (each containing 35 patients). Group A received IV dexmedetomidine infusion (0.5 μg/kg) over 40 min and Group B received intranasal dexmedetomidine (1 μg/kg) 40 min before induction. It was concluded that both intravenous and intranasal route were equally effective for blunting haemodynamic stress response. No incidence of significant bradycardia, tachycardia, hypertension, or hypotension in either group was seen.

Kochhar et al. [32] conducted a study on 90 ASA status I, adult patients, aged between 18-60 years, undergoing elective surgery under general anesthesia requiring endotracheal intubation. Patients were divided into three groups of 30 each. Group C received intranasal saline (2 mL), Group D1 and Group D2 received intranasal dexmedetomidine (1 μg/ kg) and (2 μg/kg), respectively, diluted in 2 mL saline 30 minutes before the induction of anesthesia. In this study, it was observed that all haemodynamic parameters remained below baseline even after intubation in patients who were premedicated with intranasal dexmedetomidine. Requirement of propofol for induction in patients sedated with intranasal dexmedetomidine was decreased. However, intranasal dexmedetomidine 2μg/ kg was associated with a higher incidence of bradycardia.

A study was conducted by Nagesh Panditrao et al. [33] for evaluation of intranasal dexmedetomidine as a premedication for attenuating hemodynamic stress response to laryngoscopy and intubation. A study was done on 60 patients scheduled for elective CABG under general anaesthesia, divided in two groups of 30 patients each. Group A (Lignocaine group): Patient received injection Xylocard 2% (Lignocaine, 1.5 mg/kg) 90 seconds prior to induction. Group D (Dexmedetomidine group): Patients Intranasal 2μg/kg Dexmedetomidine 60 min. prior to induction. It was concluded that intranasal Dexmedetomidine in the dose of 2 μg/kg significantly blunted the haemodynamic response to tracheal intubation and can maintain stable haemodynamics.

Ola M. Zanaty et al. [18] (2015) conducted study on 60 children, aged 3-6 years, ASA I and II for comparison of nebulised dexmedetomidine, nebulised ketamine and their combination as premedication for outpatient paediatric dental surgery and concluded that a nebulised combination of low dose dexmedetomidine and ketamine produced more satisfactory sedation and provided more smooth induction of general anaesthesia, with more rapid recovery and no significant side effects.

A study was conducted by Satyajeet Misra et al. [10] on 120 ASA I and II patients on effect of pre-operative dexmedetomidine nebulisation on haemodynamic response to laryngoscopy and intubation. Group 1 (control) patients received 0.9% saline nebulisation (3–4 ml), Group 2 patients received 1 μg/kg dexmedetomidine nebulisation diluted in 3–4 ml of 0.9% saline, 30 min before induction of anesthesia. It was concluded that nebulised dexmedetomidine 1μg/kg had significant effect on attenuation of increase in HR but not SBP following laryngoscopy. 1μg/kg nebulised dexmedetomidine also reduced the intraoperative anaesthetic and analgesic consumption as compared to control group. No effect on

early postoperative nausea vomiting, sore-throat or increase incidence of adverse effects were seen.

Nimmagadda R Kumar et al. [1] (2020) conducted a study on 100 ASA I, II patients, on evaluation of nebulised dexmedetomidine(1μg/kg) in comparison to normal saline (control group) in blunting haemodynamic response to intubation. It was found that in dexmedetomidine group, there was a statistically significant decrease in MAP after intubation as compared to control group and a statistically significant intra-group decline in MAP as compared to the baseline (before nebulisation) after laryngoscopy and intubation. In this study SBP, DBP also significantly decreased after laryngoscopy and intubation in dexmedetomidine group but no significant difference in the HR was seen. There was a dose sparing effect of propofol in a group which received nebulised dexmedetomidine(1μg/kg) than control group. No adverse effects were seen in dexmedetomidine group

Priyanka Shrivastava et al. [2] (2022) conducted a study on 100 patients with the ASA I and II patients divided into two groups: group A (n = 50) included patients nebulised with dexmedetomidine 1 μg/kg and group B (n = 50) included patients nebulised with 5 ml saline 30 minutes before induction of anaesthesia, to study the effect of nebulised dexmedetomidine at a dose of 1 μg /kg in reducing the stress response to laryngoscopy and intubation. It was concluded that in patients who received dexmedetomidine nebulisation, there was statistically significant blunting of SBP, DBP, MAP and HR following intubation. Dose sparing effect on the induction dose of propofol was also seen in dexmedetomidine group. No incidence of hypotension or bradycardia seen.

Chhaya Suryawansh et al. [34] conducted study on 60 ASA 1 & 2 adult patients undergoing elective surgeries under general anaesthesia. Patients were divided into two equal groups. Group A patients were nebulised with dexmedetomidine (1µg/kg in 3-4 mL NS) and Group B patients were nebulised with normal saline (4 ml) 30 min before the induction of anaesthesia. It was found that there was significant attenuation of SBP, DBP, MAP and HR following laryngoscopy and intubation in dexmedetomidine group. There was also lower incidence of postoperative sore throat with preoperative dexmedetomidine nebulisation. No adverse effect like hypotension or bradycardia seen in either group.

In a study conducted by Mumtaz et al. [35] on 70 ASA I-II patients aged between 18 and 50 years, the efficacy of nebulised dexmedetomidine (2µg/kg) was compared with nebulisation with normal saline for blunting haemodynamic response to laryngoscopy and intubation. It was shown that even though dexmedetomidine was administered in high dose (2µg/kg) but through nebulised route rather than intravenous, resulted in attenuation of increased HR, SBP, DBP and MAP in response to laryngoscopy and intubation as compared to control group. No side effect was seen in dexmedetomidine group. This study was limited to only five minutes post intubation.

In previous studies, there were conflicting results related to haemodyamic responses with nebulisation with 1µg/kg of dexmedetomidine. So, we plan to compare pre-operative nebulisation with 1µg/kg and 2µg/kg of dexmedetomidine to find out the optimal dose with minimal side effects for blunting hemodynamic response to laryngoscopy and intubation.

MATERIALS AND METHODS

SOURCE OF DATA

After approval of the Institutional ethics committee of Dayanand Medical College and Hospital, Ludhiana, the study was performed on a total of 165 adult patients scheduled for elective operative procedure under general anaesthesia with endotracheal intubation.

METHOD OF COLLECTION OF DATA

A prospective, randomized, double blind clinical study was conducted on ASA I and II patients. A total of 165 patients were recruited in the study and the patients were randomly allocated to either of the three study groups of 55 patients each by computer generated random numbers contained in sealed, sequentially numbered envelopes, which were opened by an independent anaesthesiologist.

INCLUSION CRITERIA

- Age more than 18 years
- ASA I &II patients
- Patient with Mallampati class 1 or 2

EXCLUSION CRITERIA

- Pregnant females
- Patient with unstable haemodynamics
- Predicted airway difficulty
- ASA III & IV patients
- Known allergy to dexmedetomidine

GROUP ALLOCATION:

A total of 165 adult patients undergoing surgery under general anaesthesia with tracheal intubation were recruited for the study and were randomly allocated using a computer-generated random number list into

three groups of 55 patients, each using consecutively numbered opaque sealed envelopes.

GROUP 0 [control group] :(n=55)

Patients were nebulised for ten-minutes with 5 ml of solution containing 0.9% Sodium Chloride (NaCl), ten-minutes before induction.

GROUP I: **(n=55)**

Patients were nebulised for ten-minutes with 5 ml of solution containing 1µg/kg of dexmedetomidine in 0.9% NaCl, ten-minutes before induction.

GROUP II: (n=55)

Patients were nebulised for ten-minutes with 5 ml of solution containing 2µg/kg of dexmedetomidine in 0.9% NaCl, ten-minutes before induction.

PRE-ANAESTHETIC CHECKUP

A thorough pre-anaesthetic check-up was conducted comprising of detailed history, comorbidities, allergy to any drug being used, general physical and systemic examination. Patients were explained about the study being conducted and written informed consent was taken. Relevant investigations were sent and reviewed. Demographic information including height, weight, BMI, age, sex, was recorded.

ANAESTHESIA TECHNIQUE

On the day of surgery patient was shifted to the operating room (OR) and standard monitors applied such as 5-lead electrocardiogram, non-invasive blood pressure (NIBP), pulse oximetry, and capnography and baseline parameters recorded. Patients were positioned on operating table in supine position and intravenous (IV) access secured and IV crystalloids started. Baseline Heart Rate (HR), Oxygen Saturation (SpO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded. The drug prepared for nebulisation was then delivered by using a nebulisation mask for ten-minutes, with the help of a wall attached oxygen driven source at a flow rate of 5-6 litres/minute.

Factors such as HR, SBP, DBP and MAP were recorded at 5^{th} and 10^{th} minute during nebulisation. Post nebulisation haemodynamic parameters were recorded at 5^{th} and 10^{th} minute.

After completion of ten-minutes after nebulisation with dexmedetomidine, patient was premedicated with injection midazolam 0.05mg/kg and metoclopramide 10mg. Patient was pre-oxygenated with 100% oxygen at flow of 10 litres/minute for 3-5 minutes with tight fitting appropriate sized face-mask. General anaesthesia was induced with intravenous (IV) fentanyl 2µg/kg and titrated dose of 1% propofol intravenously till the patient's verbal response was abolished. Neuromuscular blockade was achieved by using injection atracurium 0.5mg/kg intravenously. Pre-intubation haemodynamic parameters were recorded. After 150 seconds an experienced anaesthesiologist performed a laryngoscopy, and appropriately sized, styleted, endotracheal tube (ETT) was inserted in trachea, cuff inflated and connected to ventilator. After confirmation of correct placement and checking equal bilateral air entry, the ETT was secured. Lungs were mechanically ventilated using volume-controlled ventilation using 35% oxygen in nitrous oxide (N_2O) and 1.5% Isoflurane.

Haemodynamic parameters were recorded immediately after intubation, and then after every one minute for first ten-minutes. After ten-minutes of intubation, the surgeon was allowed to proceed for surgery. The anaesthesiologist was allowed to manage anaesthetic care of the patient during surgery as per institutional protocol. At end of procedure neuromuscular blockade was reversed using intravenous (IV) injections of neostigmine 0.05mg/kg and glycopyrrolate 0.02mg/kg and ETT was removed after confirming return of spontaneous and normal pattern of ventilation. Patient was then shifted to post-anaesthesia care unit for observation.

Outcome:

Primary outcome:

- To find most effective dose of nebulised dexmedetomidine with minimal side effect in blunting haemodynamic response to laryngoscopy and intubation by comparing HR, SBP, DBP and MAP at pre-induction, pre-intubation, after-intubation and up to 10 minutes post intubation.

Secondary Outcome:

- To compare effect of 1 & 2 µg/kg nebulised dexmedetomidine on reduction of induction dose of propofol.
- To compare incidence and magnitude of complication associated with use of 1 & 2 µg/kg nebulised dexmedetomidine.

STATISTICAL ANALYSIS

Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using ANOVA. For comparing categorical data, Chi square ($\chi 2$) test was performed and Fischer exact test was used when the expected frequency was less than 5. A probability value (p value) less than 0.05 was be considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

SAMPLE SIZE CALCULATION

A post hoc power analysis was conducted using the software package, G*Power version 3.1.9.2 (Franz Faul, university Kiel, Germany). The alpha level used for this analysis was $p<0.05$ and beta was 0.20. Sample size was estimated from the results of previous study [1]

using MAP at one- minute as the parameter, which is the primary outcome of our study. Our sample size came out to be 50 subjects per group at power of 0.99 and with an effect size of 1.65 with 10% chance of error with $\alpha = 0.05$, $\beta = 0.20$ and confidence interval of 95%.

Total cases 150. To allow for a possible dropout rate of 10%, a total of 165 patients were recruited.

OBSERVATIONS AND RESULTS

The present randomized control study was conducted in a prospective manner in the department of Anesthesiology, DMCH Ludhiana on a total of 165 patients scheduled for elective procedures under general anaesthesia with endotracheal intubation belonging to ASA grade I and II. The study aimed to compare the effect of pre-operative nebulisation with 1µg/kg and 2µg/kg of dexmedetomidine to find an optimal dose for blunting hemodynamic response to laryngoscopy and intubation.

Figure (A): CONSORT Flow Diagram of the study

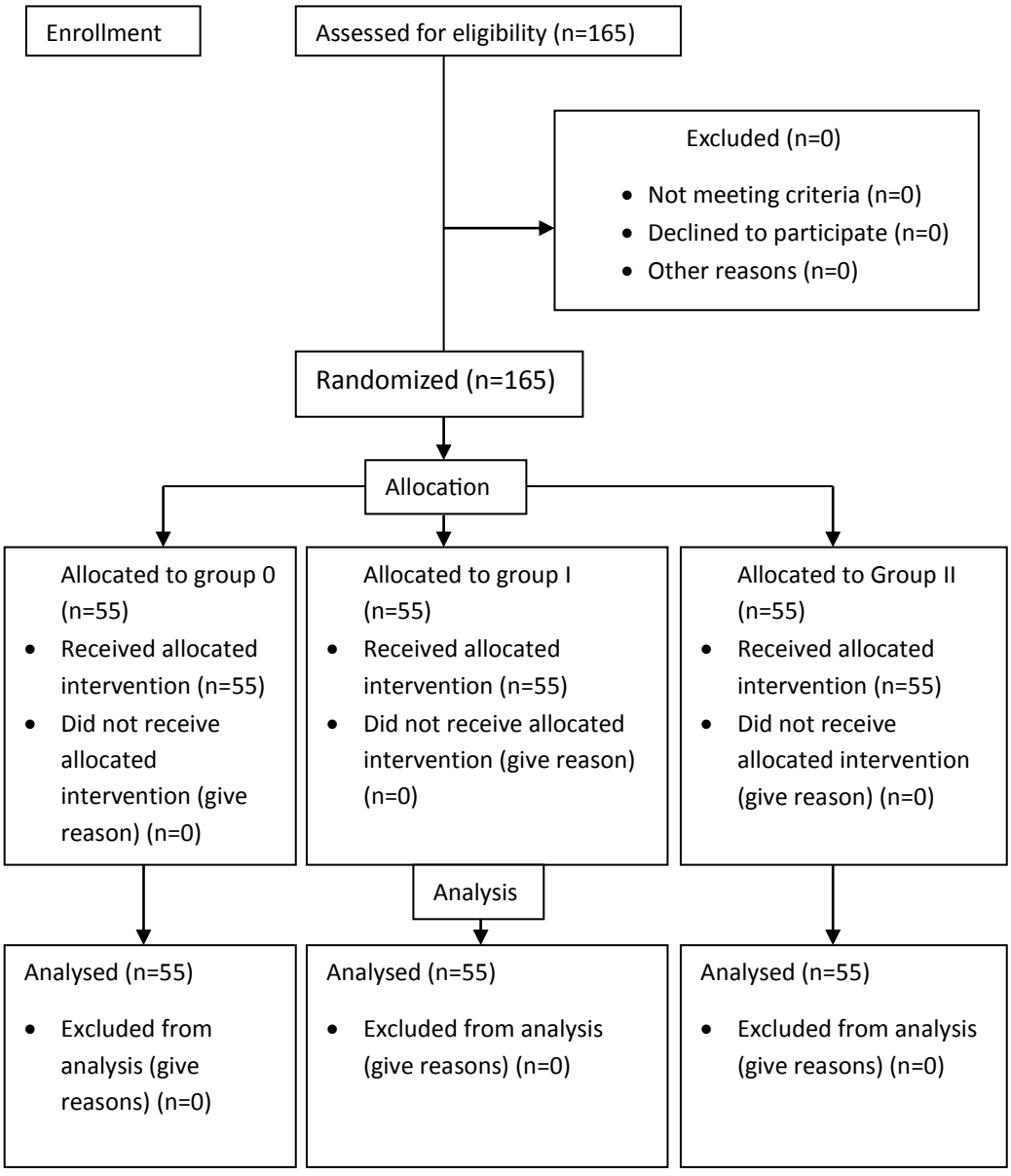
Enrollment
Assessed for eligibility (n=165)
Excluded (n=0)
Not meeting criteria (n=0)
Declined to participate (n=0)
Other reasons (n=0)
Randomized (n=165)
Allocation
Allocated to group 0 (n=55)
Received allocated intervention (n=55)
Did not receive allocated intervention (give reason) (n=0)
Allocated to group I (n=55)
Received allocated intervention (n=55)
Did not receive allocated intervention (give reason) (n=0)
Allocated to Group II (n=55)
Received allocated intervention (n=55)
Did not receive allocated intervention (give reason) (n=0)
Analysis
Analysed (n=55)
Excluded from analysis (give reasons) (n=0)
Analysed (n=55)
Excluded from analysis (give reasons) (n=0)
Analysed (n=55)
Excluded from analysis (give reasons) (n=0)

Table 1: Distribution of patients according to age (years)

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
Age (years)	39.49	12.89	37.25	11.90	42.22	15.10	1.903	0.152

The three groups were comparable with respect to age. Mean age in group 0 was 39.49±12.89 years, 37.25±11.90 years in group I and 42.2±15.10 years in group II

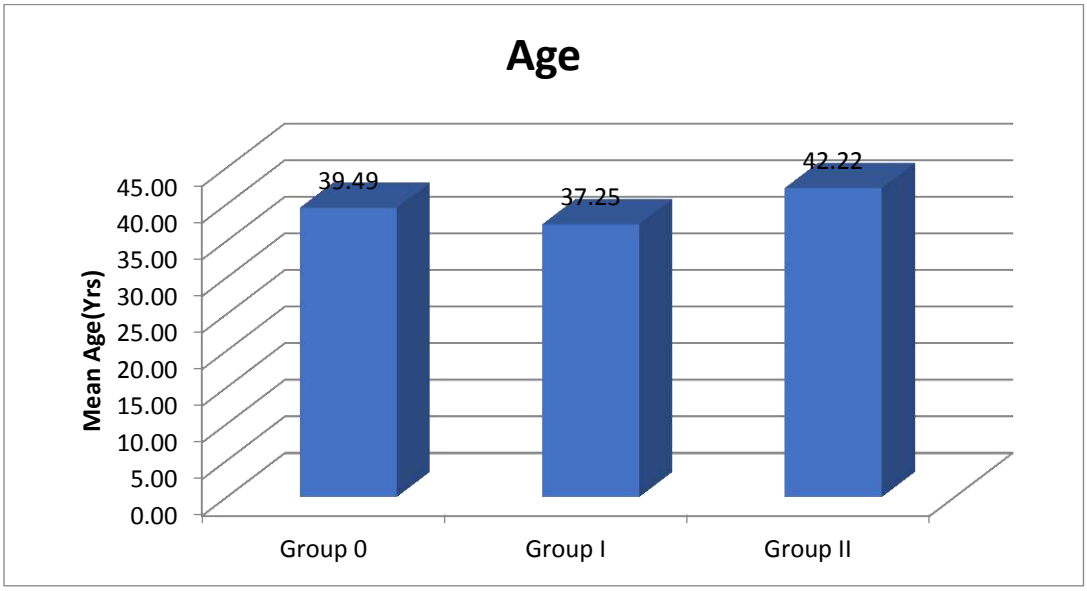

Figure 1: Distribution of patients according to age (years)

Table 2: Distribution of patients according to height (m), weight (kg), BMI (kg/m^2)

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
height (m)	1.64	0.07	1.65	0.08	1.63	0.08	1.444	0.239
Weight (Kg)	67.36	11.84	70.51	12.97	69.49	12.53	0.913	0.403
BMI (Kg/m2)	25.05	3.60	25.69	3.90	26.12	4.18	1.040	0.356

The groups were comparable with respect to height (m), weight (Kg), BMI(Kg/m2). The mean height in group 0 was 1.64 m, 1.65 m in group I and 1.63 m in group II.

Similarly, mean weight in group 0 was 67.36 kg, 70.51 kg in group I and 69.49 kg in group II.

Mean BMI(kg/m2) in group 0 was 25.05 kg/m^2, 25.69 kg/m^2 in group I and 26.12 kg/m^2 in group II.

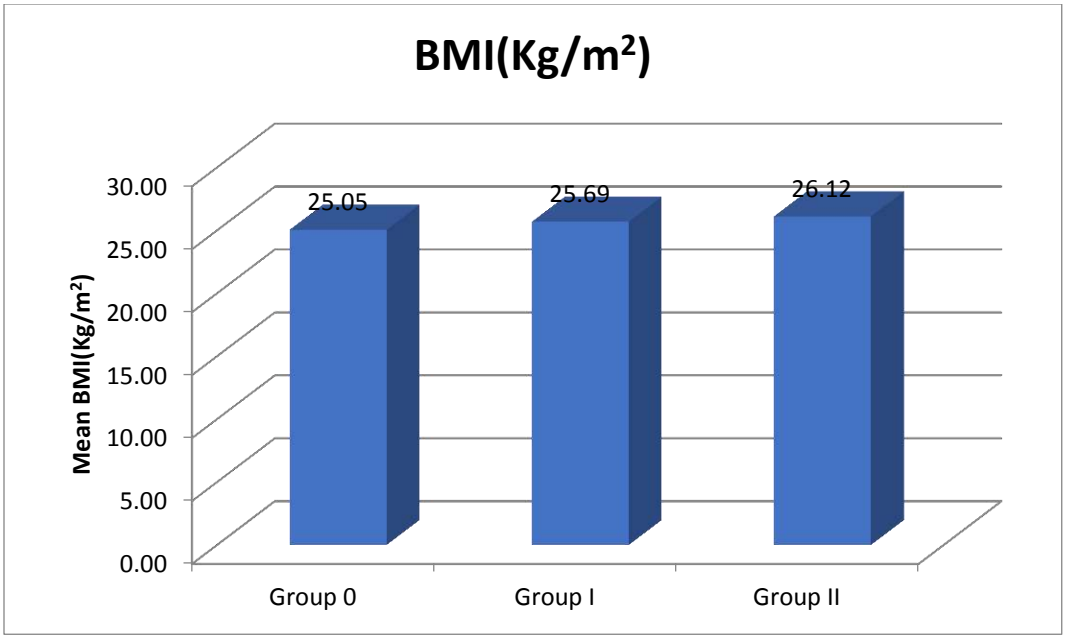

Figure 2: Distribution of patients according to BMI(Kg/m^2)

Table 3: Distribution of patients according to gender

		Group 0		Group I		Group II		Total	Chi-square value	p-value
		Group 0	Group 0	Group I	Group I	Group II	Group II			
Sex	F	30	54.5%	31	56.4%	32	58.2%	93	0.148	0.929
	M	25	45.5%	24	43.6%	23	41.8%	72		
Total		55	100.0%	55	100.0%	55	100.0%	165		

The three groups were comparable with respect to gender, however there were more of female patients as compared to males in all the three groups. In group 0, there were 54.5% females and 45.5% males, in group I there were 56.4% females and 43.6% males, in group II, there were 58.2% females and 41.8% males.

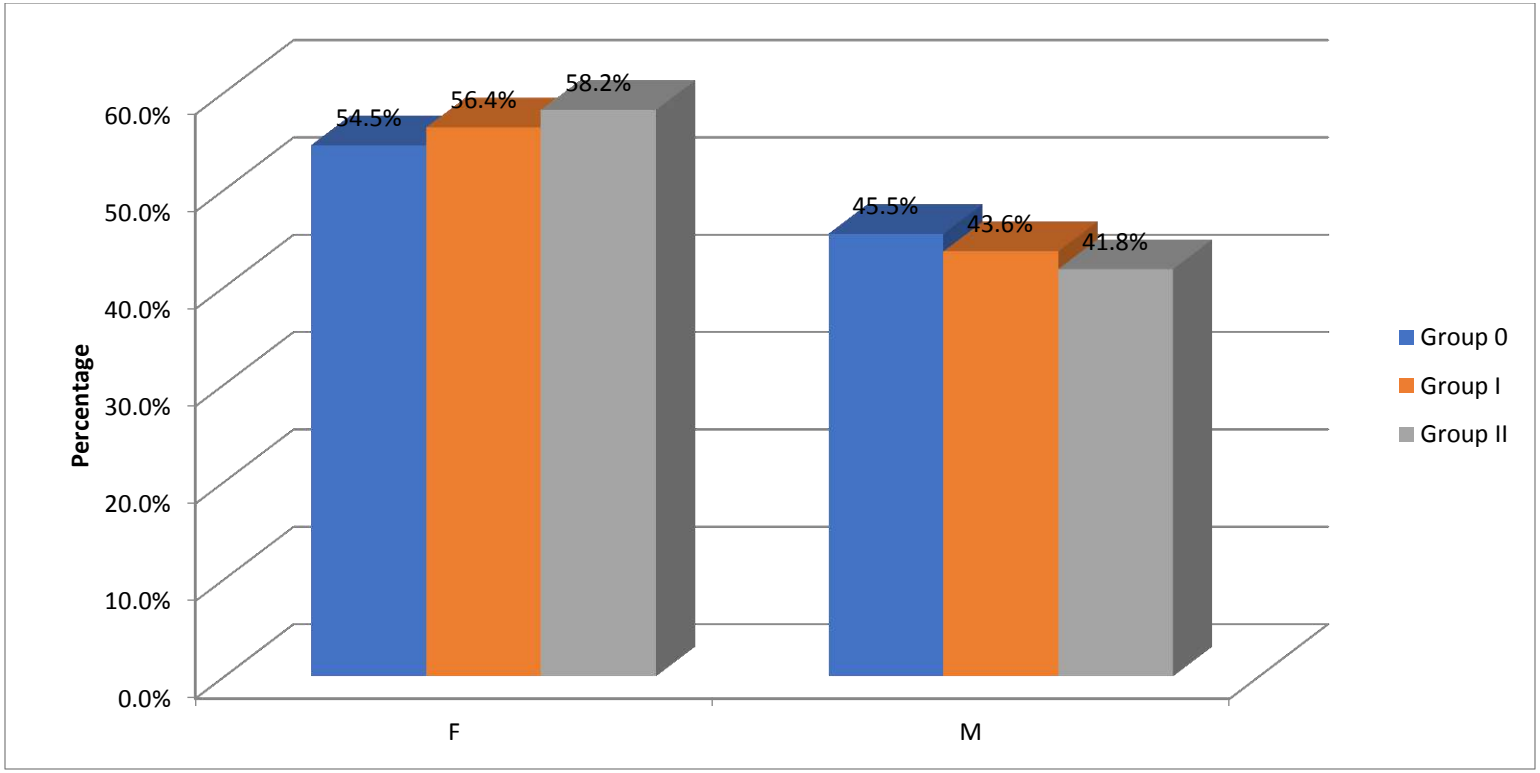

Figure 3: Distribution of patients according to gender

Table 4: Distribution of patients according to ASA grading

		Group 0		Group I		Group II		Total	Chi-square value	p-value
		Group 0	Group 0	Group I	Group I	Group II	Group II			
ASA grade	I	46	83.6%	45	81.8%	46	83.6%	137	0.086	0.958
	II	9	16.4%	10	18.2%	9	16.4%	28		
Total		55	100.0%	55	100.0%	55	100.0%	165		

The three groups were comparable with respect to ASA grading. 83.6% of patients of group 0, 81.8% of patients of group I and 83.6% of patients of group II belonged to ASA I. 16.4% of patients of group 0, 18.2% of patients of group I and 16.4% of patients of group II belonged to ASA II.

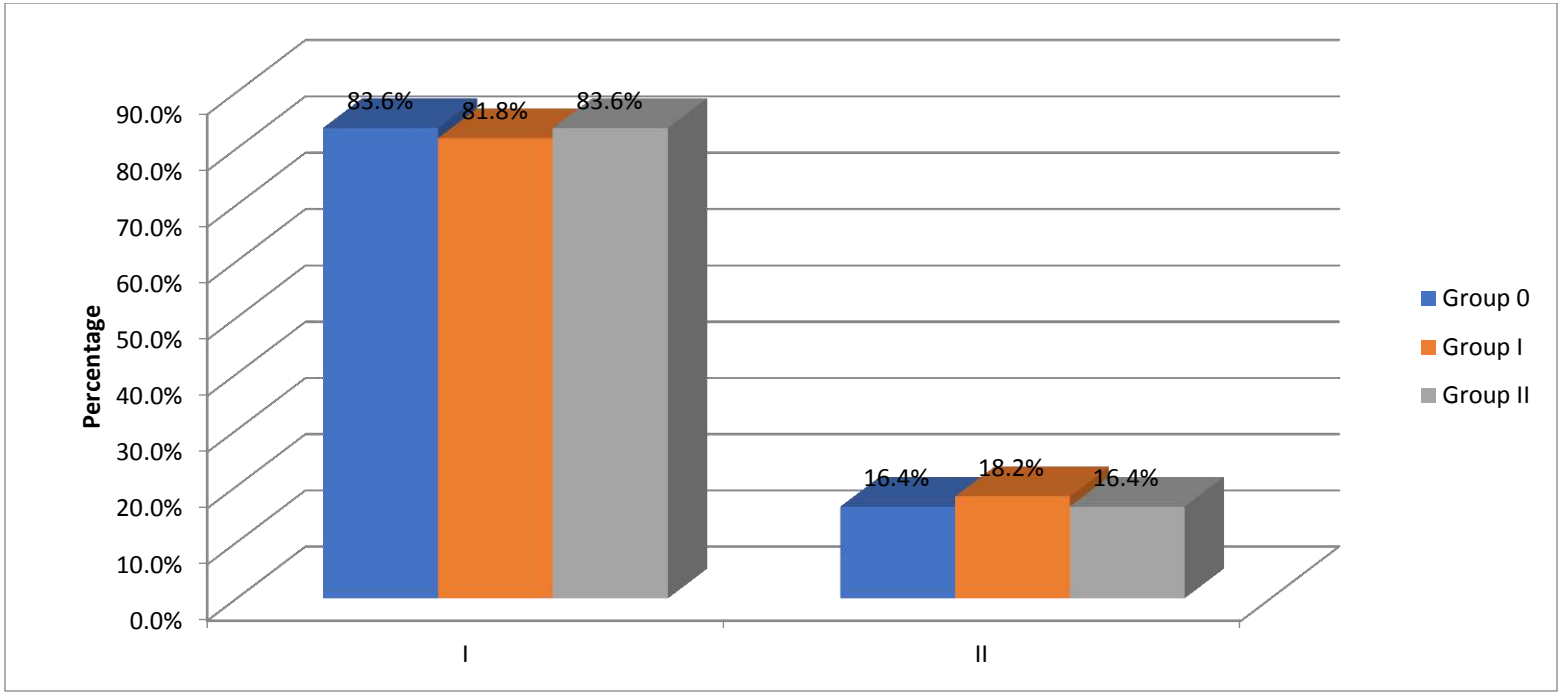

Figure 4: Distribution of patients in 3 groups according to ASA grading

Table 5: Distribution of patients according to Mallampati grading

		Group 0		Group I		Group II		Total	Chi-square value	p-value
		Group 0	Group 0	Group I	Group I	Group II	Group II			
Mallampati class	1	21	38.2%	17	30.9%	19	34.5%	57	0.643	0.725
	2	34	61.8%	38	69.1%	36	65.5%	108		
Total		55	100.0%	55	100.0%	55	100.0%	165		

The three groups were comparable with respect to Mallampati grading. 38.2% of patients in Group 0, 30.9% of patients in Group I and 34.5% of patients in Group II had MPS 1. 61.8% of patients in Group 0, 69.1% of patients in Group I and 65.5% of patients in Group II had MPS 2. This difference was however not statistically significant.

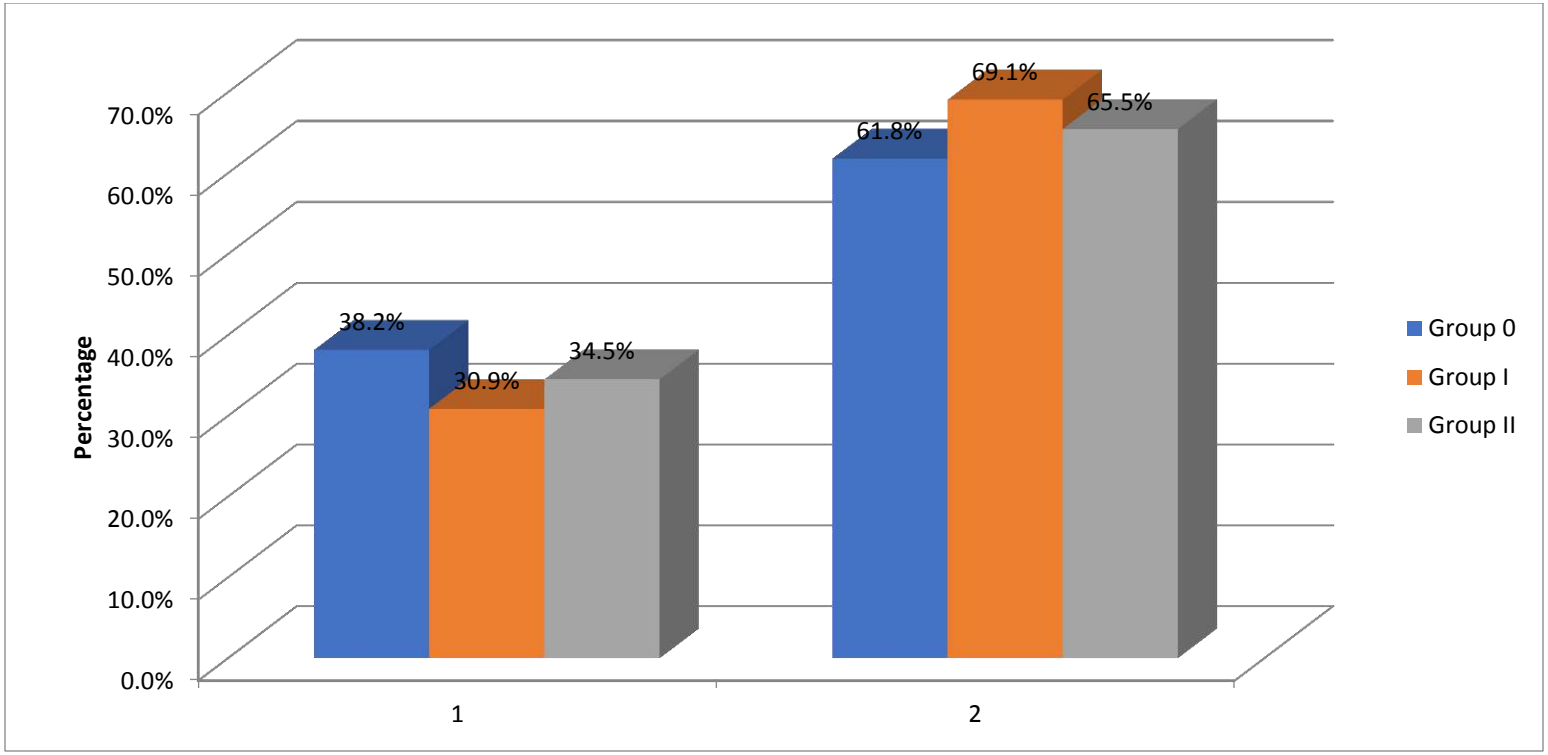

Figure 5: Distribution of patients according to Mallampati grading in three groups

Table 6: Distribution of patient according to comorbidities

		Group 0		Group I		Group II		Total	Chi-square value	p-value
		Group 0	Group 0	Group I	Group I	Group II	Group II			
	No	48	87.3%	45	81.8%	46	83.6%	139		
Comorbidities	Anaemia	1	1.8%	1	1.8%	0	0.0%	2	16.693	0.544
	Chronic Alcoholic	0	0.0%	1	1.8%	0	0.0%	1		
	Chronic Smoker	1	1.8%	0	0.0%	0	0.0%	1		
	Hypertension	3	5.5%	3	5.5%	2	3.6%	8		
	Hypothyroid	1	1.8%	1	1.8%	5	9.1%	7		
	Overweight	0	0.0%	2	3.6%	0	0.0%	2		
	Type 2 Diabetes Mellitus	1	1.8%	2	3.6%	2	3.6%	5		
Total		55	100.0%	55	100.0%	55	100.0%	165		

Out of 55 patients in Group 0, 87.3% of patients had no comorbidities, 1.8% of patients had anaemia, 1.8% of patients were chronic smoker, 5.5% of patients had hypertension (HTN), 1.8% of patients had hypothyroidism and 1.8% of patients had type2 diabetes mellitus (T2DM)

Similarly, out of 55 patients in Group I, 81.8% of patients had no comorbidities, 1.8% of patients had anaemia, 1.8% of patients were chronic alcoholic, 5.5% of patients had HTN, 1.8% of patients had hypothyroidism, 3.6% of patients had T2DM and 3.6% of patients were overweight

Similarly, out of 55 patients in Group II, 83.6% of patients had no comorbidities, 3.6% of patients had HTN, 9.09% of patients had hypothyroidism and 3.6% of patients had T2DM.

This difference was however not statistically significant.

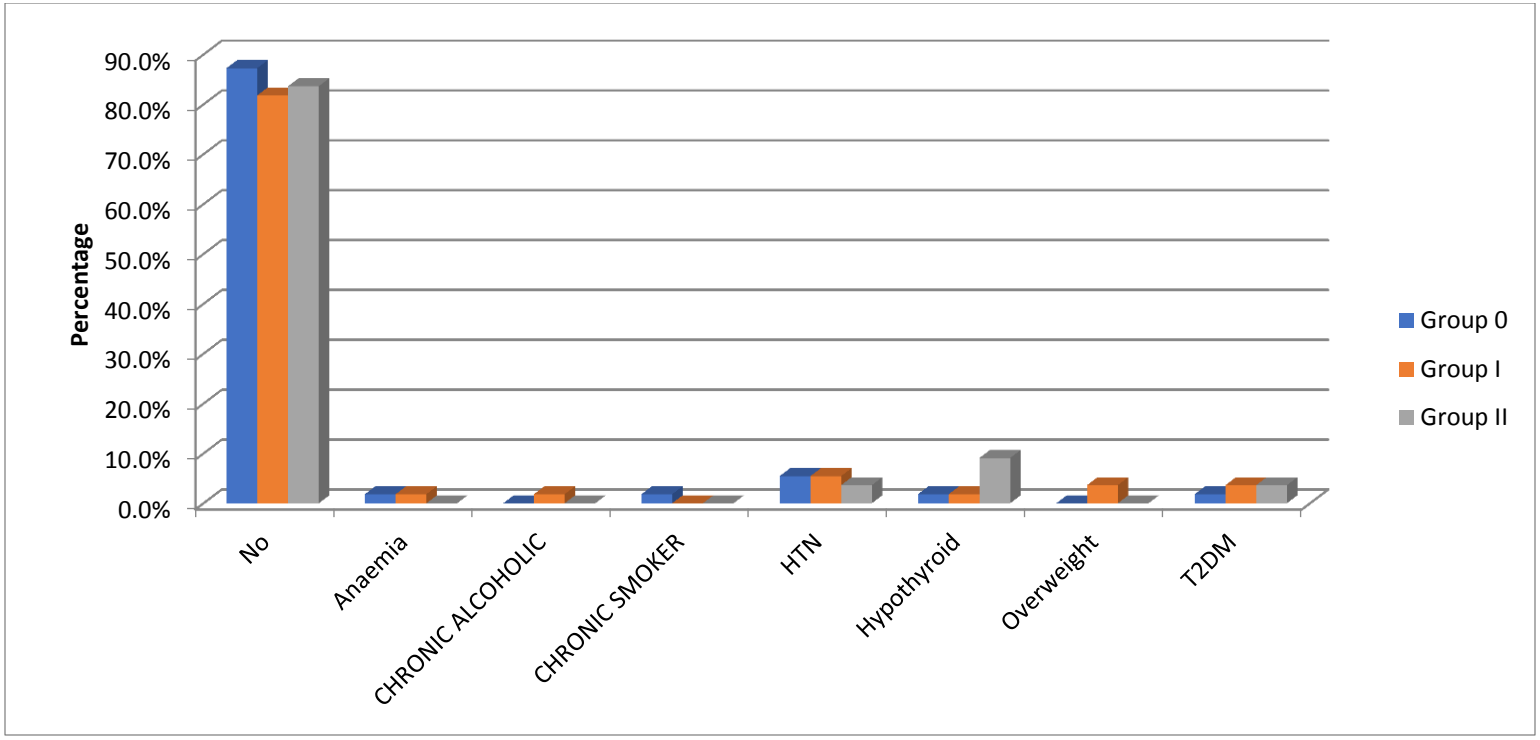

Figure 6: Distribution of patient according to comorbidities

Table 7: Intra-group comparison of heart rate in relation to baseline (Before nebulisation) at different time points.

	Group 0		p-value	Group I		p-value	Group II		p-value
	Mean	SD		Mean	SD		Mean	SD	
Heart Rate Before nebulisation	82.04	12.17		81.84	10.69		81.60	11.35	
Heart Rate Just before intubation	74.69	11.72	0.000	71.98	8.47	0.000	72.45	10.99	0.000
Heart Rate Immediately after intubation	99.09	12.08	0.000	88.75	10.51	0.000	85.05	11.16	0.000
Heart Rate_1 min	97.07	12.54	0.000	86.24	10.32	0.000	83.42	10.85	0.039
Heart Rate_2 min	95.96	12.85	0.000	84.18	10.38	0.070	81.75	10.66	0.880
Heart Rate_3 min	94.64	12.96	0.000	83.04	10.19	0.335	79.91	10.19	0.069
Heart Rate_4 min	93.25	12.54	0.000	82.18	9.69	0.765	79.18	10.26	0.018
Heart Rate_5 min	91.27	12.46	0.000	80.93	9.75	0.434	78.02	10.12	0.000
Heart Rate_6 min	89.76	12.24	0.000	80.00	9.66	0.102	77.07	9.76	0.000
Heart Rate_7 min	88.69	12.03	0.000	79.00	9.86	0.020	75.78	9.48	0.000
Heart Rate_8 min	86.96	12.00	0.000	78.07	9.74	0.001	74.93	9.22	0.000
Heart Rate_9 min	84.93	11.37	0.019	77.04	9.48	0.000	73.76	9.26	0.000
Heart Rate_10 min	83.24	11.03	0.299	75.56	9.19	0.000	72.96	9.73	0.000

Baseline mean heart rate (HR) were comparable among three groups. The mean HR significantly increased from baseline, at immediately after intubation in Group 0, which remained significantly higher till nine minutes. In both Group I and II mean heart rate significantly increased immediately after intubation and remained significantly higher till one minute.

Table 8: Comparison of heart rate in three groups at different time points.

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
Heart Rate Before nebulisation	82.04	12.17	81.84	10.69	81.60	11.35	0.020	0.980
Heart Rate During Nebulisation 5 min	81.82	12.19	80.75	10.08	79.84	11.25	0.431	0.651
Heart Rate During Nebulisation 10 min	81.93	11.78	79.87	9.76	79.15	10.86	0.976	0.379
Heart Rate After Nebulisation 5th min	81.71	11.99	77.85	13.87	77.82	10.70	1.831	0.164
Heart Rate After Nebulisation 10th min	81.89	12.33	78.29	9.39	78.29	11.16	1.931	0.148
Heart Rate Just before intubation	74.69	11.72	71.98	8.47	72.45	10.99	1.047	0.353
Heart Rate Immediately after intubation	99.09	12.08	88.75	10.51	85.05	11.16	22.692	0.000
Heart Rate_1 min	97.07	12.54	86.24	10.32	83.42	10.85	22.468	0.000
Heart Rate_2 min	95.96	12.85	84.18	10.38	81.75	10.66	24.686	0.000
Heart Rate_3 min	94.64	12.96	83.04	10.19	79.91	10.19	26.444	0.000
Heart Rate_4 min	93.25	12.54	82.18	9.69	79.18	10.26	25.431	0.000
Heart Rate_5 min	91.27	12.46	80.93	9.75	78.02	10.12	22.698	0.000
Heart Rate_6 min	89.76	12.24	80.00	9.66	77.07	9.76	21.525	0.000
Heart Rate_7 min	88.69	12.03	79.00	9.86	75.78	9.48	22.459	0.000
Heart Rate_8 min	86.96	12.00	78.07	9.74	74.93	9.22	19.853	0.000
Heart Rate_9 min	84.93	11.37	77.04	9.48	73.76	9.26	17.819	0.000
Heart Rate_10 min	83.24	11.03	75.56	9.19	72.96	9.73	15.640	0.000

The mean HR recorded before nebulisation (baseline), during nebulisation (5 minute, 10 minute), after nebulisation (5 minute, 10minute) and before intubation were comparable in all three groups ($p>0.05$). The mean HR immediately after laryngoscopy and intubation and at every one minute till ten minutes after intubation were higher in Group 0 when compared to Group I and Group II. This difference was statistically significant with p value< 0.05.

However, on comparing group I and II, there was no statistically significant difference in mean HR immediately after laryngoscopy and intubation and at every one minute till ten minutes after intubation ($p>0.05$).

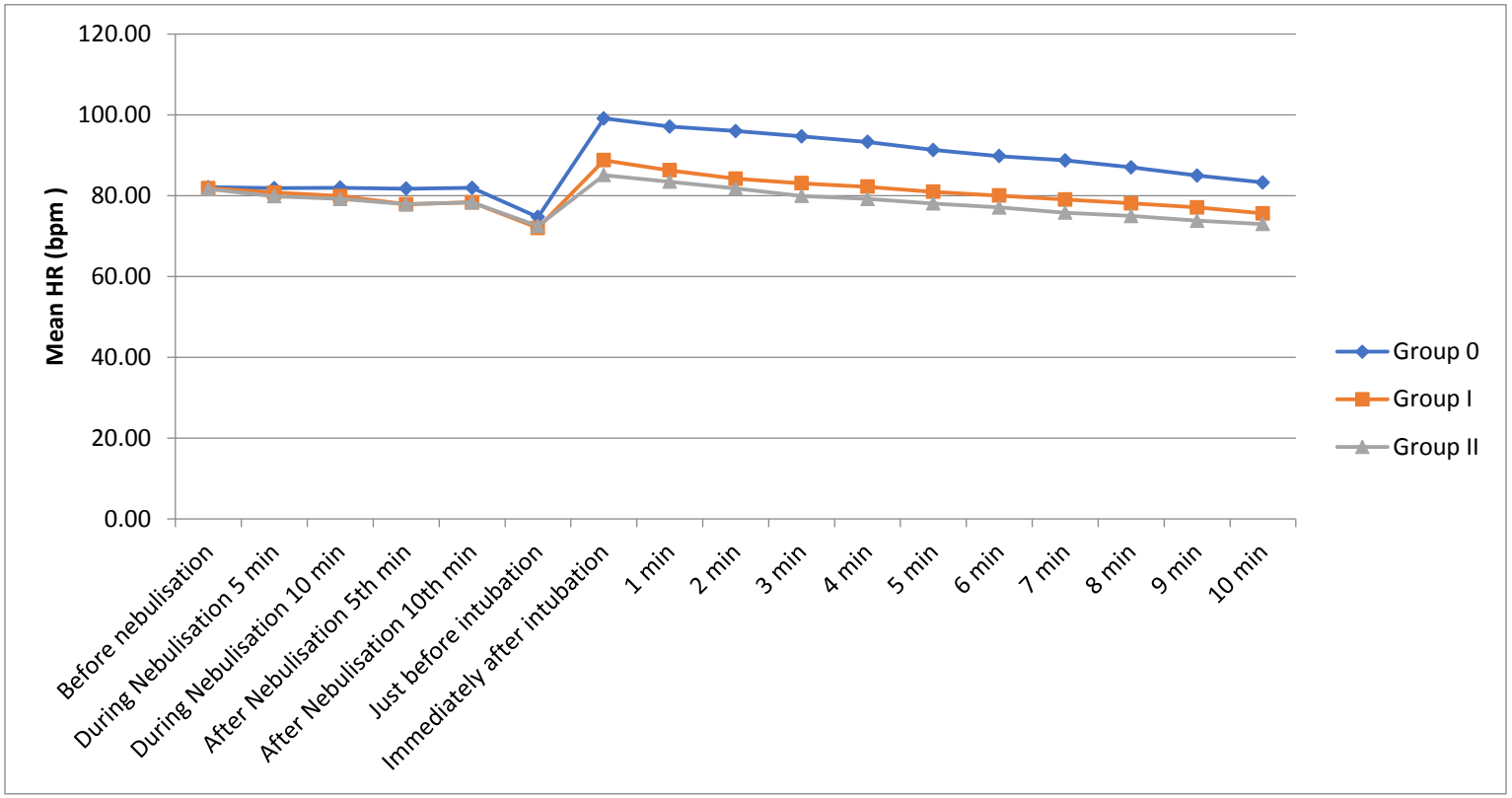

Figure 7: Distribution of heart rate in three groups at different time points .

Table 9: Intra-group comparison of systolic blood pressure in relation to baseline (Before nebulisation) at different time points

	Group 0		p-value	Group I		p-value	Group II		p-value
	Mean	SD		Mean	SD		Mean	SD	
SBP_Before nebulisation	121.62	12.00		124.51	9.29		124.15	10.34	
SBP_Just before intubation	105.36	10.37	0.000	107.24	7.91	0.000	107.38	10.16	0.000
SBP_Immediately after intubation	136.07	9.66	0.000	128.51	7.83	0.000	123.91	9.09	0.848
SBP_1 min	133.25	8.60	0.000	125.40	7.77	0.408	121.44	8.91	0.032
SBP_2 min	130.69	9.48	0.000	123.64	8.94	0.510	119.11	8.60	0.000
SBP_3 min	128.42	8.78	0.000	121.91	8.20	0.047	117.27	7.37	0.000
SBP_4 min	126.15	9.01	0.008	120.36	7.97	0.001	115.60	8.27	0.000
SBP_5 min	124.53	8.28	0.070	117.76	7.81	0.000	114.93	7.47	0.000
SBP_6 min	122.20	7.96	0.724	116.42	7.72	0.000	113.80	7.99	0.000
SBP_7 min	120.64	7.60	0.530	115.11	7.79	0.000	112.29	8.05	0.000
SBP_8 min	118.65	7.51	0.053	114.02	7.91	0.000	110.64	7.61	0.000
SBP_9 min	116.76	7.36	0.001	112.78	7.78	0.000	112.13	8.31	0.000
SBP_10 min	114.91	7.58	0.000	110.84	8.46	0.000	108.07	8.59	0.000

Baseline mean systolic blood pressure (SBP) were comparable among three groups. The mean SBP significantly increased from baseline, immediately after intubation in Group 0, which remained significantly higher till four minutes. In Group I mean SBP significantly increased immediately after intubation and remained significantly higher till one minute. Mean SBP was significantly lower than baseline from three minute after intubation and remained significantly lower at all intervals thereafter, in Group I. In Group II, mean SBP was nearly same as baseline immediately after intubation. Mean SBP was significantly lower than baseline from one minute after intubation and remained significantly lower at all intervals thereafter, in Group II.

Table 10: Distribution of systolic blood pressure (SBP) in three groups at different time points.

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
SBP_Before nebulisation	121.62	12.00	124.51	9.29	124.15	10.34	1.213	0.300
SBP_During Nebulisation 5 min	121.11	11.15	122.96	8.81	123.78	10.13	1.016	0.364
SBP_During Nebulisation 10 min	121.30	10.84	121.89	8.24	121.84	10.65	0.929	0.397
SBP_After Nebulisation 5th min	119.20	17.01	121.09	8.66	119.55	9.15	0.373	0.689
SBP_After Nebulisation 10th min	119.22	11.24	119.55	8.04	117.36	9.72	0.800	0.451
SBP_Just before intubation	105.36	10.37	107.24	7.91	107.38	10.16	0.765	0.467
SBP_Immediately after intubation	136.07	9.66	128.51	7.83	123.91	9.09	26.236	0.000
SBP_1 min	133.25	8.60	125.40	7.77	121.44	8.91	27.936	0.000
SBP_2 min	130.69	9.48	123.64	8.94	119.11	8.60	23.058	0.000
SBP_3 min	128.42	8.78	121.91	8.20	117.27	7.37	26.019	0.000
SBP_4 min	126.15	9.01	120.36	7.97	115.60	8.27	21.587	0.000
SBP_5 min	124.53	8.28	117.76	7.81	114.93	7.47	21.658	0.000
SBP_6 min	122.20	7.96	116.42	7.72	113.80	7.99	16.331	0.000
SBP_7 min	120.64	7.60	115.11	7.79	112.29	8.05	16.225	0.000
SBP_8 min	118.65	7.51	114.02	7.91	110.64	7.61	15.130	0.000
SBP_9 min	116.76	7.36	112.78	7.78	112.13	8.31	5.652	0.004
SBP_10 min	114.91	7.58	110.84	8.46	108.07	8.59	9.618	0.000

The mean SBP recorded before nebulisation (baseline) during nebulisation (5-minute, 10 minute) after nebulisation (5 minute, 10minute) before intubation, were comparable in all three groups ($p>0.05$). The mean SBP immediately after laryngoscopy and intubation and at every one minute till ten minutes after intubation were higher in Group 0 when compared to Group I and Group II and this difference was statistically significant with p value< 0.05.The mean SBP immediately after laryngoscopy and intubation, at every one minute till four minutes after intubation were higher in Group I when compared to Group II and this

difference was statistically significant with p value< 0.05. At 5th to 10th minutes after intubation, mean SBP were comparable in Group I and Group II.

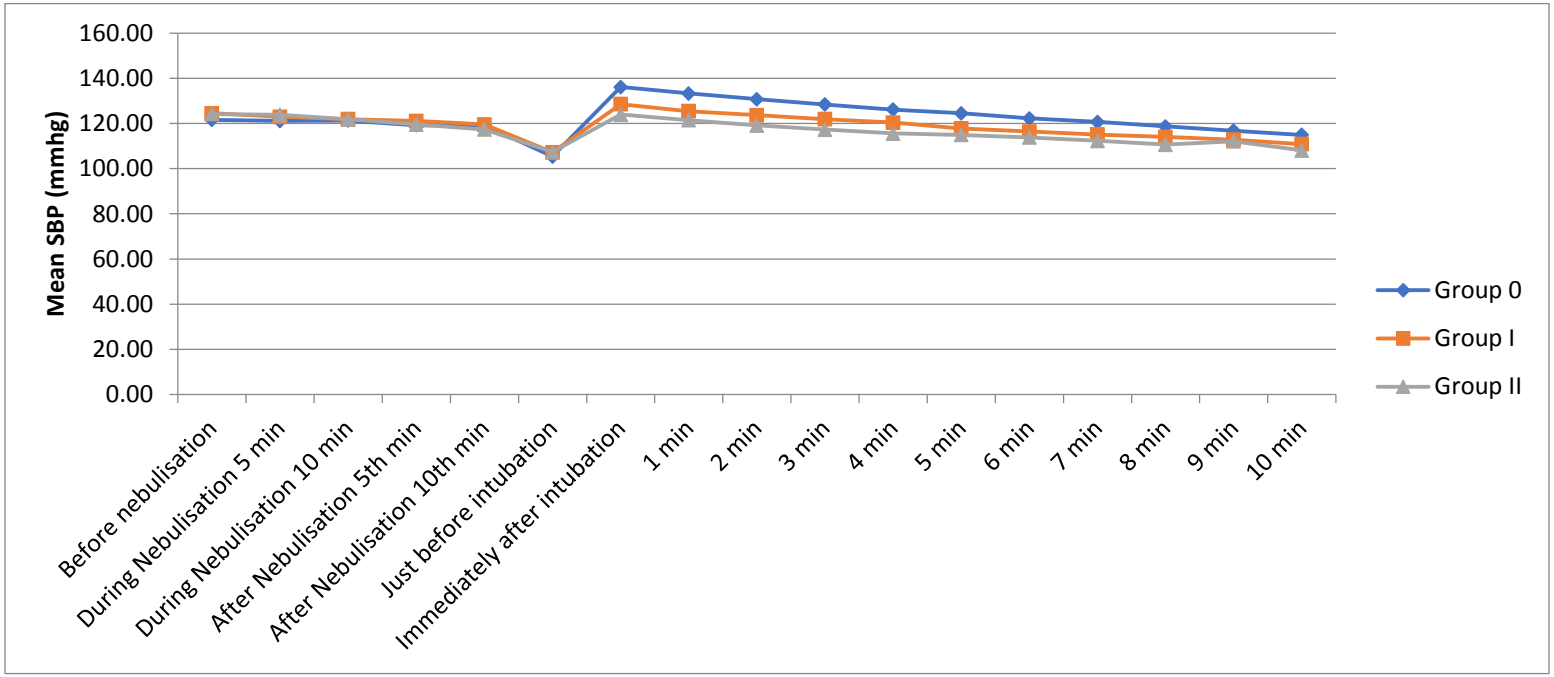

Figure 8: Distribution of SBP in three groups at different time points.

Table 11: Intra-group comparison of diastolic blood pressure (DBP) in relation to baseline (Before nebulisation) at different time points

	Group 0		p-value	Group I		p-value	Group II		p-value
	Mean	SD		Mean	SD		Mean	SD	
DBP_Before nebulisation	70.93	9.70		73.25	9.11		73.38	9.46	
DBP_Just before intubation	61.53	7.68	0.000	62.38	6.78	0.000	61.80	7.70	0.000
DBP_Immediately after intubation	80.04	11.22	0.000	75.35	10.02	0.043	75.36	8.68	0.063
DBP_1 min	76.85	10.08	0.000	72.27	8.43	0.349	71.38	7.35	0.064
DBP_2 min	75.00	9.17	0.000	70.07	8.14	0.016	69.93	6.51	0.001
DBP_3 min	73.04	8.99	0.042	68.31	7.53	0.000	68.60	6.83	0.000
DBP_4 min	71.55	8.66	0.550	66.98	7.82	0.000	66.87	6.87	0.000
DBP_5 min	70.53	8.48	0.708	67.56	7.62	0.000	65.51	7.04	0.000
DBP_6 min	69.93	7.79	0.391	66.60	7.12	0.000	65.04	6.19	0.000
DBP_7 min	68.15	8.02	0.021	65.51	5.97	0.000	64.36	6.60	0.000
DBP_8 min	67.15	6.89	0.002	62.13	6.27	0.000	62.85	10.82	0.000
DBP_9 min	65.67	6.80	0.000	62.44	5.61	0.000	62.91	6.17	0.000
DBP_10 min	63.80	6.48	0.000	62.18	6.04	0.000	61.91	6.82	0.000

Baseline mean diastolic blood pressure (DBP) were comparable among three groups. The mean DBP significantly increased from baseline, at immediately after intubation in Group 0, which remained significantly higher till three minutes. In Group I mean SBP significantly increased immediately after intubation and thereafter started decreasing. Mean DBP was significantly lower than baseline from two minutes after intubation and remained significantly lower at all intervals thereafter, in Group I. In Group II, although mean DBP increased immediately after intubation but it was lower than baseline, which was not significant. Mean DBP was significantly lower than baseline from two minute after intubation and remained significantly lower at all intervals thereafter, in Group II.

Table 12: Distribution of diastolic blood pressure (DBP) in three groups at different time points.

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
DBP_Before nebulisation	70.93	9.70	73.25	9.11	73.38	9.46	1.182	0.309
DBP_During Nebulisation 5 min	70.24	8.48	71.71	8.56	71.42	8.90	0.447	0.640
DBP_During Nebulisation 10 min	70.38	8.81	70.93	7.83	72.80	8.16	1.291	0.278
DBP_After Nebulisation 5th min	70.51	8.95	70.05	8.57	71.69	8.65	0.515	0.598
DBP_After Nebulisation 10th min	69.35	8.23	69.07	7.85	69.60	7.93	0.060	0.942
DBP_Just before intubation	61.53	7.68	62.38	6.78	61.80	7.70	0.191	0.826
DBP_Immediately after intubation	80.04	11.22	75.35	10.02	75.36	8.68	3.996	0.020
DBP_1 min	76.85	10.08	72.27	8.43	71.38	7.35	6.273	0.002
DBP_2 min	75.00	9.17	70.07	8.14	69.93	6.51	7.147	0.001
DBP_3 min	73.04	8.99	68.31	7.53	68.60	6.83	6.286	0.002
DBP_4 min	71.55	8.66	66.98	7.82	66.87	6.87	6.400	0.002
DBP_5 min	70.53	8.48	67.56	7.62	65.51	7.04	5.852	0.004
DBP_6 min	69.93	7.79	66.60	7.12	65.04	6.19	6.878	0.001
DBP_7 min	68.15	8.02	65.51	5.97	64.36	6.60	4.326	0.015
DBP_8 min	67.15	6.89	62.13	6.27	62.85	10.82	5.956	0.003
DBP_9 min	65.67	6.80	62.44	5.61	62.91	6.17	4.359	0.014
DBP_10 min	63.80	6.48	62.18	6.04	61.91	6.82	1.380	0.255

The mean DBP recorded before nebulisation (baseline), during nebulisation (5 minute, 10 minute), after nebulisation (5 minute, 10minute) and before intubation were comparable in all three groups ($p>0.05$). The mean DBP immediately after laryngoscopy and intubation, at every one minute till nine minutes after intubation were higher in Group 0 when compared to Group I and Group II. This difference was statistically significant with p value< 0.05. Whereas, the mean DBP immediately after laryngoscopy and intubation, at every one minute till ten minutes after intubation were comparable in Group I and Group II ($p>0.05$).

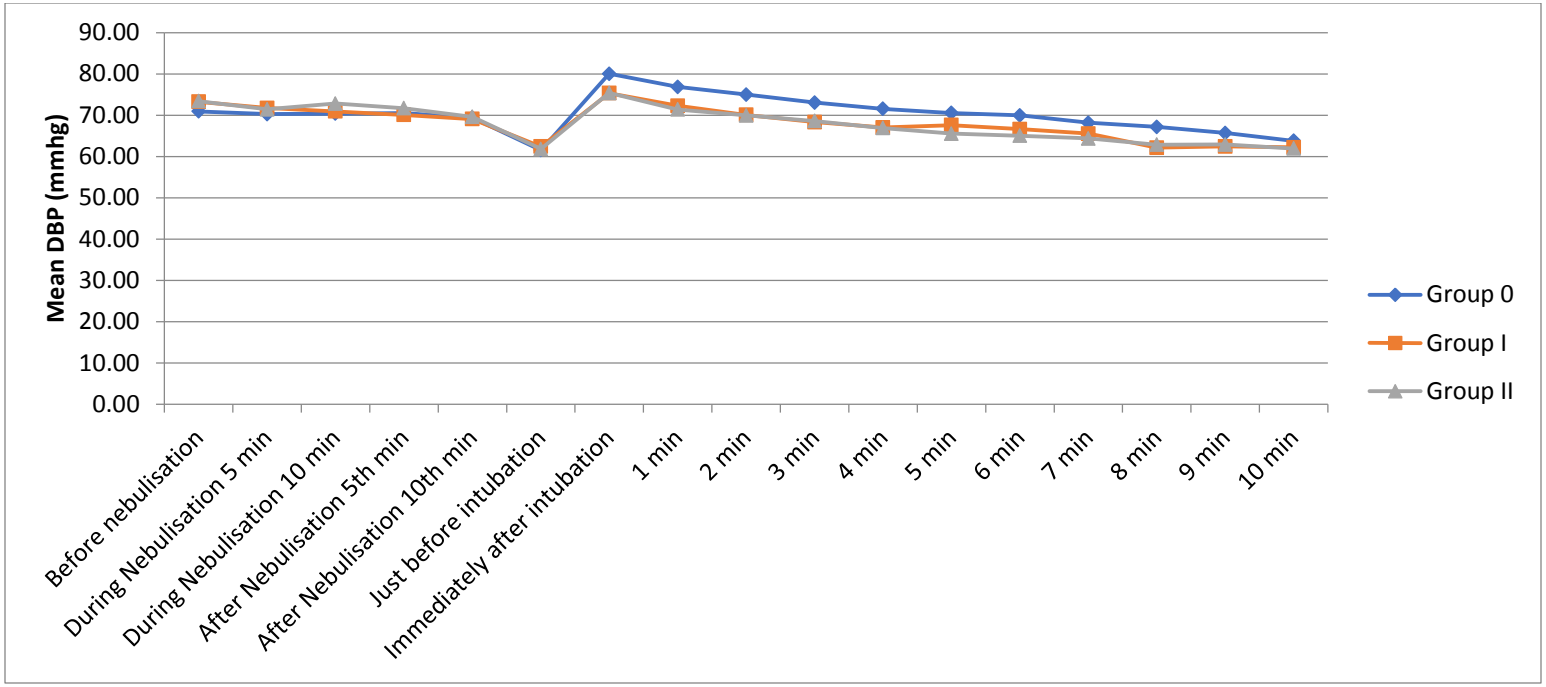

Figure 9: Distribution of DBP in three groups at different time points.

Table 13: Intra-group comparison of mean arterial pressure (MAP) in relation to baseline (Before nebulisation) at different time points

	Group 0		p-value	Group I		p-value	Group II		p-value
	Mean	SD		Mean	SD		Mean	SD	
MAP_Before nebulisation	87.82	9.22		90.34	8.10		90.30	8.20	
MAP_Just before intubation	76.14	7.23	0.000	77.33	5.77	0.000	76.99	7.26	0.000
MAP_Immediately after intubation	98.72	9.76	0.000	93.07	8.28	0.001	91.55	7.60	0.189
MAP_1 min	95.65	8.66	0.000	89.98	7.05	0.695	88.07	6.69	0.029
MAP_2 min	93.56	8.06	0.000	87.93	7.42	0.051	86.32	5.71	0.000
MAP_3 min	91.50	7.71	0.001	86.18	6.71	0.000	84.82	5.52	0.000
MAP_4 min	89.75	7.56	0.073	84.78	6.77	0.000	83.12	5.98	0.000
MAP_5 min	88.53	7.46	0.514	84.30	6.58	0.000	81.98	5.78	0.000
MAP_6 min	87.35	6.45	0.673	83.21	6.48	0.000	81.29	5.36	0.000
MAP_7 min	85.64	6.58	0.051	82.04	5.67	0.000	80.34	5.69	0.000
MAP_8 min	84.32	5.91	0.002	79.42	5.73	0.000	78.78	7.84	0.000
MAP_9 min	82.70	5.95	0.000	79.22	5.37	0.000	79.32	5.51	0.000
MAP_10 min	80.84	5.85	0.000	78.40	5.86	0.000	77.30	5.96	0.000

Baseline mean arterial pressure (MAP) were comparable among three groups. The MAP significantly increased from baseline, immediately after intubation in Group 0, which remained significantly higher till three minutes. In Group I MAP significantly increased immediately after intubation and thereafter started decreasing. The MAP was significantly lower than baseline from three minutes after intubation and remained significantly lower at all intervals thereafter, in Group I. In Group II, although MAP increased immediately after intubation but it was not significant. Mean MAP was significantly lower than baseline from one minute after intubation and remained significantly lower at all intervals thereafter, in Group II.

Table 14: Distribution of mean arterial pressure (MAP) in three groups at different time points

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
MAP_Before nebulisation	87.82	9.22	90.34	8.10	90.30	8.20	1.575	0.210
MAP_During Nebulisation 5 min	87.19	8.07	88.79	7.49	88.87	7.68	0.821	0.442
MAP_During Nebulisation 10 min	94.02	49.96	87.92	6.96	89.15	7.33	0.662	0.517
MAP_After Nebulisation 5th min	86.74	8.89	87.07	7.44	87.64	7.07	0.187	0.830
MAP_After Nebulisation 10th min	85.97	8.15	85.90	6.66	85.52	6.91	0.060	0.942
MAP_Just before intubation	76.14	7.23	77.33	5.77	76.99	7.26	0.452	0.637
MAP_Immediately after intubation	98.72	9.76	93.07	8.28	91.55	7.60	10.636	0.000
MAP_1 min	95.65	8.66	89.98	7.05	88.07	6.69	15.164	0.000
MAP_2 min	93.56	8.06	87.93	7.42	86.32	5.71	15.645	0.000
MAP_3 min	91.50	7.71	86.18	6.71	84.82	5.52	15.228	0.000
MAP_4 min	89.75	7.56	84.78	6.77	83.12	5.98	14.147	0.000
MAP_5 min	88.53	7.46	84.30	6.58	81.98	5.78	13.732	0.000
MAP_6 min	87.35	6.45	83.21	6.48	81.29	5.36	14.095	0.000
MAP_7 min	85.64	6.58	82.04	5.67	80.34	5.69	11.217	0.000
MAP_8 min	84.32	5.91	79.42	5.73	78.78	7.84	11.695	0.000
MAP_9 min	82.70	5.95	79.22	5.37	79.32	5.51	6.873	0.001
MAP_10 min	80.84	5.85	78.40	5.86	77.30	5.96	5.199	0.006

The MAP recorded before nebulisation (baseline), during nebulisation (5 minute, 10 minute), after nebulisation (5 minute, 10minute) and before intubation were comparable in all three groups ($p>0.05$). The MAP immediately after laryngoscopy and intubation, at every one minute till ten minutes after intubation were higher in Group 0 when compared to Group I and Group II. This difference was statistically significant with p value< 0.05.

Whereas, MAP immediately after laryngoscopy and intubation, at every one minute till ten minutes after intubation were comparable in Group I and Group II (p>0.05).

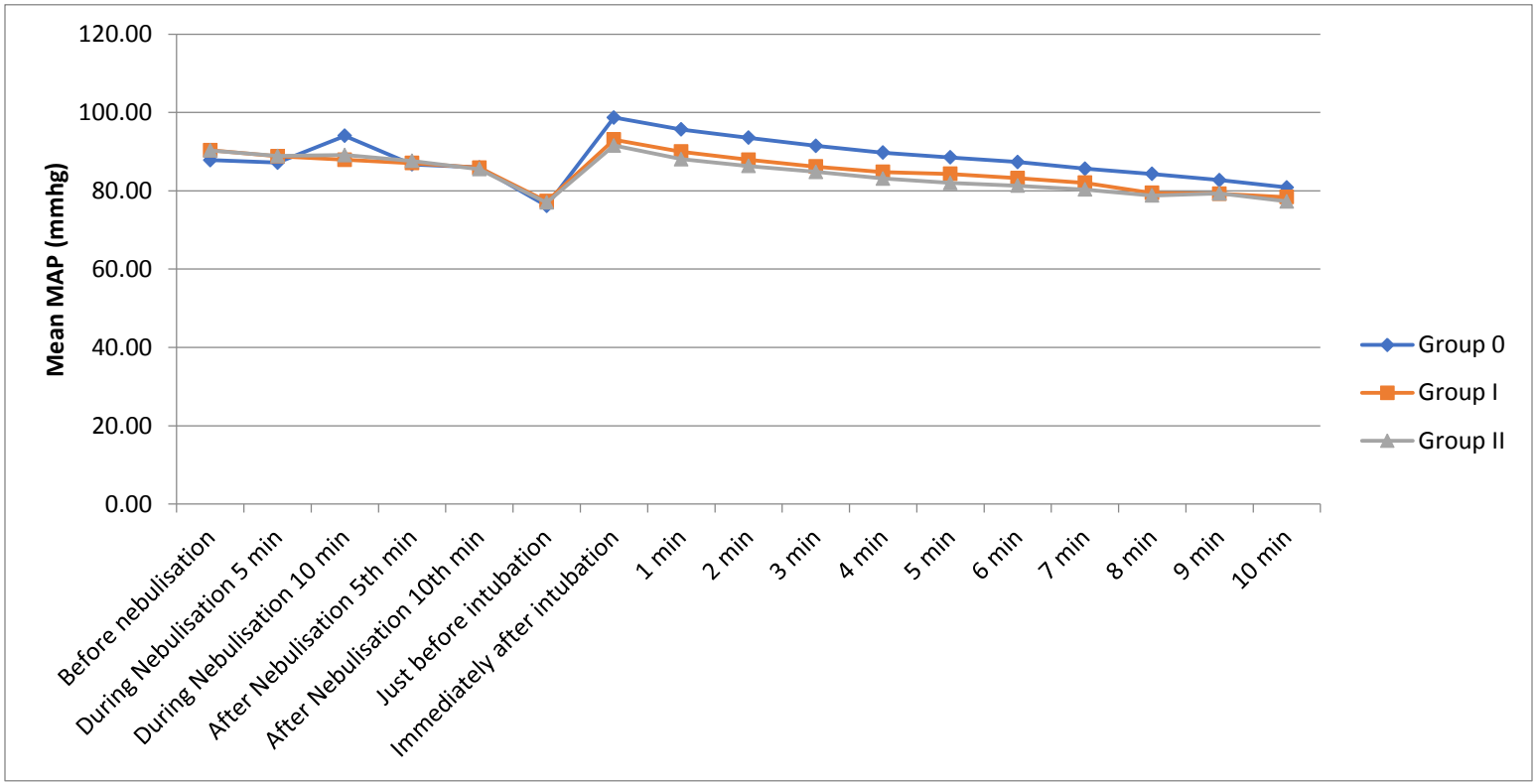

Figure 10: Distribution of MAP in three groups at different time points.

Table 15: Comparison of SpO_2 in three groups at different time points

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
SpO_2_Before nebulization	99.33	0.88	99.38	0.73	99.31	0.84	0.117	0.889
SpO_2_During Nebulisation 5 min	99.33	0.86	99.42	0.74	99.47	0.77	0.475	0.623
SpO_2_During Nebulisation 10 min	99.42	0.90	99.35	0.91	99.45	0.72	0.238	0.788
SpO_2_After Nebulisation 5th min	99.42	0.66	99.45	0.72	99.56	0.63	0.704	0.496
SpO_2_After Nebulisation 10th min	99.35	0.97	99.51	0.77	99.64	0.62	1.841	0.162
SpO_2_Just before intubation	99.69	0.60	99.60	0.70	99.70	0.65	1.735	0.180
SpO_2_Immediately after intubation	99.71	0.57	99.69	0.57	99.78	0.46	0.444	0.642
SpO_2_1 min	99.64	0.52	99.67	0.55	99.71	0.46	0.279	0.757
SpO_2_2 min	99.65	0.62	99.69	0.54	99.80	0.45	1.087	0.340
SpO_2_3 min	99.67	0.55	99.65	0.55	99.78	0.42	1.007	0.368
SpO_2_4 min	99.60	0.68	99.65	0.58	99.64	0.52	0.118	0.889
SpO_2_5 min	99.60	0.71	99.62	0.68	99.80	0.52	1.023	0.362
SpO_2_6 min	99.53	0.72	99.65	0.70	99.65	0.52	0.701	0.497
SpO_2_7 min	99.60	0.63	99.67	0.58	99.80	0.45	1.822	0.165
SpO_2_8 min	99.65	0.62	99.60	0.64	99.84	0.42	1.113	0.331
SpO_2_9 min	99.62	0.59	99.65	0.64	99.78	0.42	1.295	0.277
SpO_2_10 min	99.62	0.65	99.71	0.57	99.80	0.45	1.440	0.240

There was no significant difference in SpO_2 in all three groups before nebulisation, during nebulisation (5 minute, 10 minute) after nebulisation (5 minute, 10minute) before intubation, immediately after intubation, and at every 1 minute till 10 minute intraoperatively.

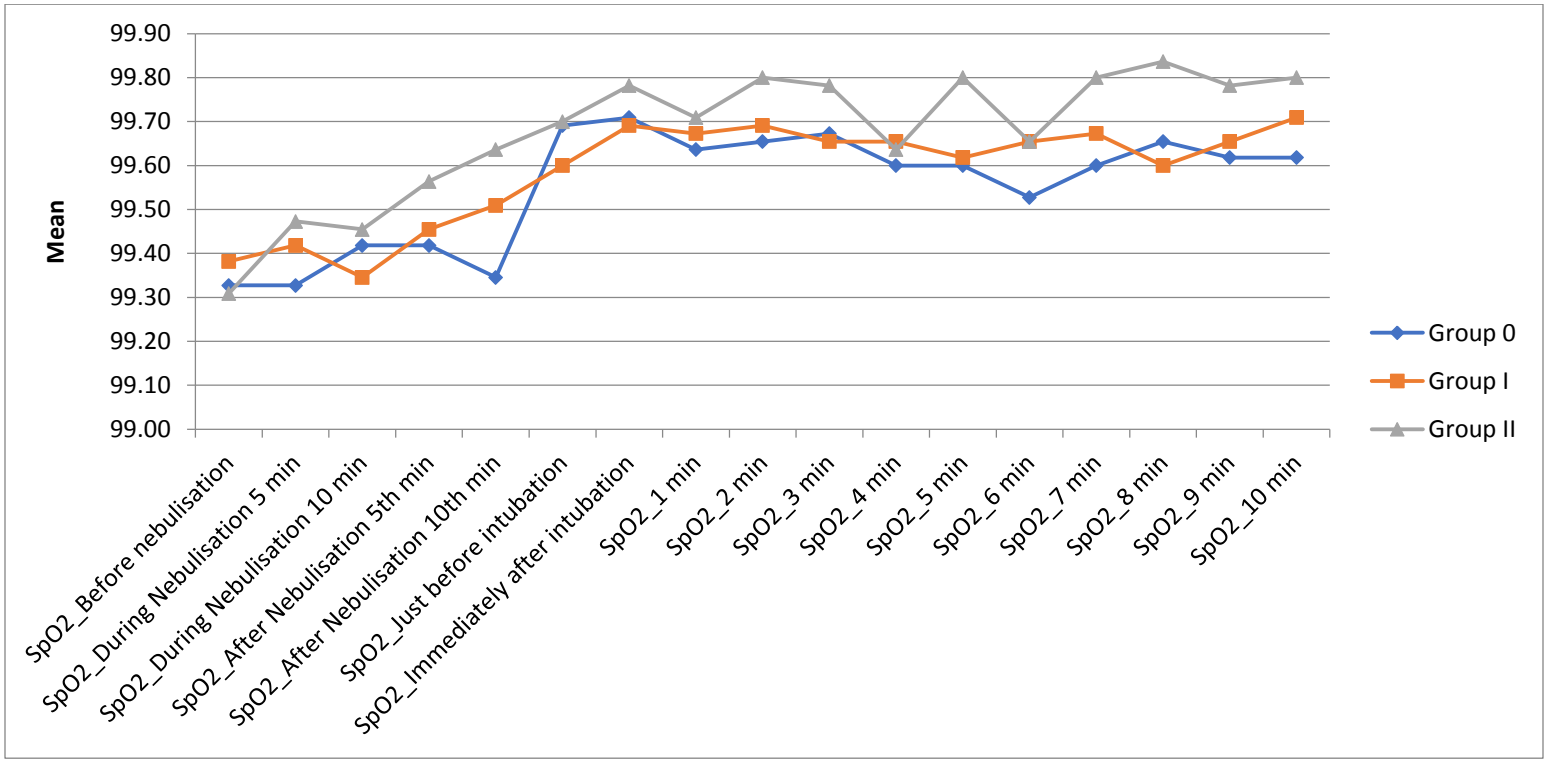

Figure 11: Comparison of SpO_2 in three groups at different time points.

Table 16: Comparison of patient based on requirement of induction dose of propofol (mg) and Time of intubation (seconds)

	Group 0		Group I		Group II		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
Induction dose of propofol (mg)	118.91	26.50	108.91	23.93	95.45	18.94	13.989	0.001
Time of intubation(secs)	14.35	1.32	14.65	1.24	14.53	1.15	0.865	0.423

There was statistically significant difference in requirement of propofol for induction in all three groups with p-value of 0.001. Requirement of propofol was least in Group II with mean of 118.91±26.50 mg as compared to Group I with mean 108.91± 23.93 mg and Group 0 with mean 95.4 ±18.94 mg. Requirement of propofol in Group I was less as compared to Group 0

All the three groups were comparable with respect to time of intubation. There was no statistically significant difference.

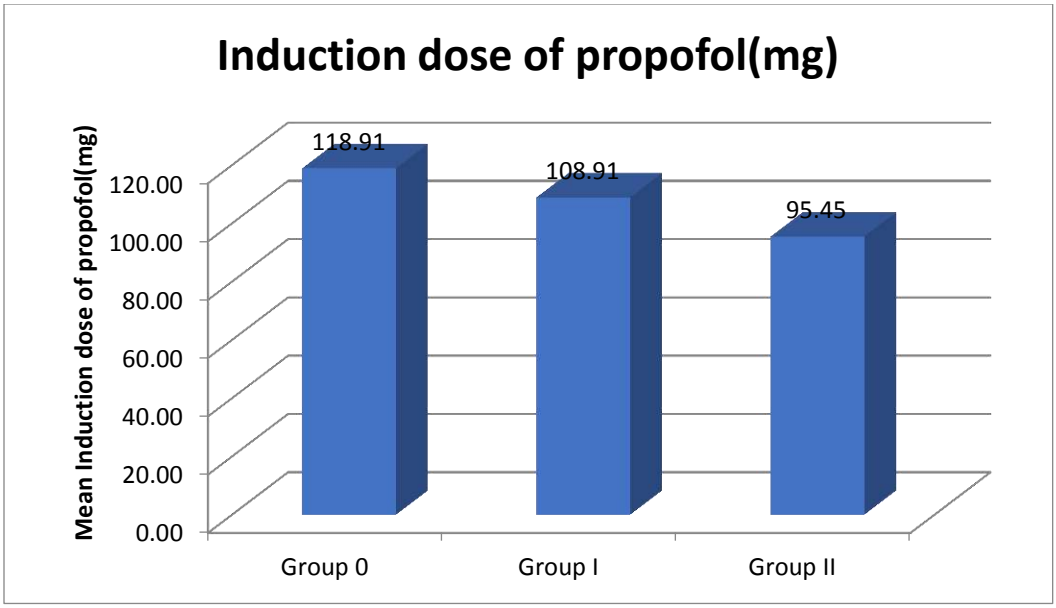

Figure 12: Comparison of patient based on requirement of induction dose of propofol

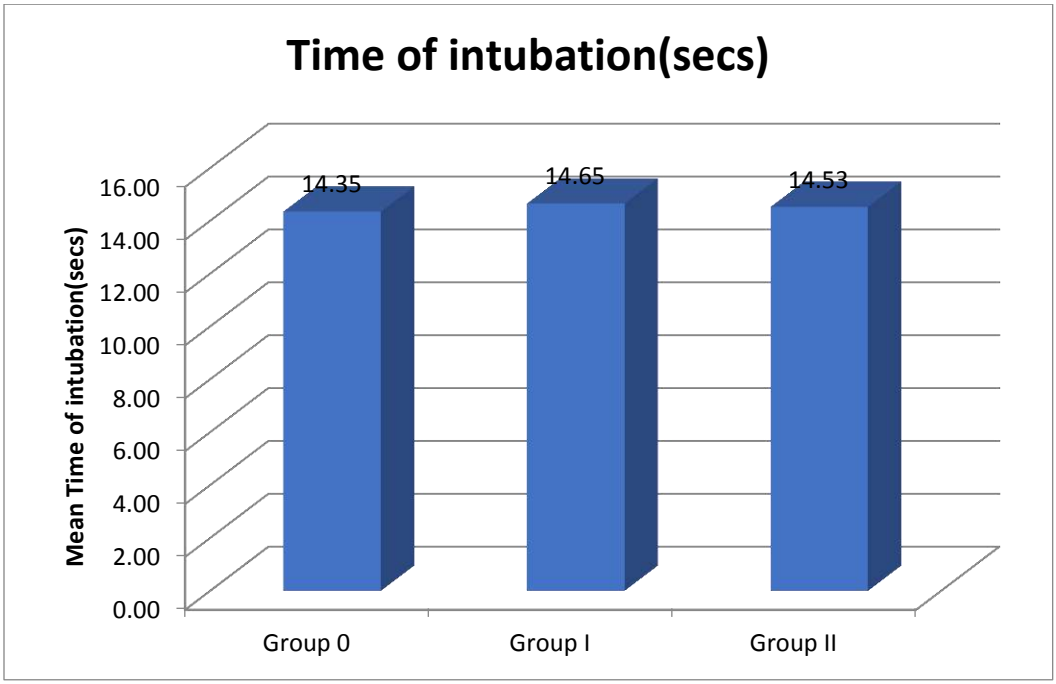

Figure 13: Comparison of patient according to Time of intubation

DISCUSSION

Stress response due to intubation and laryngoscopy can lead to tachycardia, hypertension, laryngospasm, bronchospasm, increased intracranial pressure and increased intraocular pressure. Reid and Brace [36] were the first to document the haemodynamic alterations caused by laryngoscopy and intubation. This pressor response occurs within 30 seconds after laryngoscopy and intubation and lasts for about ten minutes. [1,37] Usually, this transient response has no adverse consequences in healthy individuals. However, in patients with hypertension, coronary artery disease, myocardial insufficiency, reactive airways, and cerebrovascular diseases, it can be catastrophic leading to cardiac events like ventricular dysrhythmias, myocardial ischemia, or cerebral event like cerebrovascular stroke etc. [2,4,3,37]

Numerous drugs such as - opioids, beta- blockers, calcium channel antagonists, benzodiazepines and dexmedetomidine have been tried through different routes to attenuate the stress response to laryngoscopy and intubation but each of them has their own advantages and limitations. [1,4,10,11] The method or drug of choice depends on many factors, including the urgency of surgery, choice of anaesthetic technique, route of administration and medical condition of the patient.

Dexmedetomidine is a highly selective alpha-2 adrenergic receptor (α2-AR) agonist which has anxiolytic, anti-sialagogue, sympatholytic, cardiovascular, and neurological stabilizing properties. It has been used in various doses and through various routes of administration such as intravenous (IV), intranasal, and nebulised, for decreasing pressor response to intubation.[2] Dexmedetomidine at an IV loading dose of 0.5 and 1μg/kg, attenuates increase in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) in normal patients with heathy cardiovascular system but at the same time, IV bolus dose may lead to profound bradycardia and hypotension in cardio-compromised and hypovolemic patients.[1] Intranasal administration

of dexmedetomidine can also effectively attenuate stress response to tracheal intubation. The intra-nasal method of drug delivery is linked to brief nose discomfort, occasionally coughing, vocal cord irritation or even laryngospasm. [1,15]

The purpose of this prospective randomized study was to compare pre-operative nebulisation with 1μg/kg and 2μg/kg of dexmedetomidine to find an optimal dose with minimal side effects for blunting hemodynamic response to laryngoscopy and intubation in patients undergoing elective surgery under general anaesthesia.

The study was conducted in the Department of Anaesthesia, Dayanand Medical College and Hospital, Ludhiana on 165 ASA I and II patients posted for elective surgery under general anesthesia. Patients were enrolled and randomly allocated into three study groups of 55 patients each (Group 0, Group I and Group II) based on computer generated random numbers. The technique for general anaesthesia was standardized in all three groups. Patients in Group 0 received nebulisation with normal saline, Group I and Group II received nebulisation with 1μg/kg and 2μg/kg dexmedetomidine, respectively, ten minutes prior to induction of general anesthesia. Haemodynamic parameters were recorded by an anaesthesiologist blinded for study. HR, SBP, DBP, MAP and oxygen saturation (SpO_2) were recorded before nebulisation, during nebulisation (five-minute, ten minute), after nebulisation (five-minute, ten minute), before intubation, immediately after intubation, and at every one minute till ten minutes intraoperatively and compared among the three groups. Requirement of induction dose of propofol was also compared among these three groups.

All three groups were statistically comparable in terms of demographic data i.e., age, sex distribution, body weight, body mass index, ASA grading and airway assessment.

HEART RATE (HR)

In our study, baseline mean HR (before nebulisation) were comparable among three groups (p>0.05). In control group mean HR was significantly higher immediately after intubation than baseline values (20.25% increase) and remained significantly higher till nine-minutes post intubation. A study was conducted by Pranav A Seth et al. [38] to evaluate the effect of 1μg/kg dexmedetomidine in comparison to control group (normal saline) by nebuliser for blunting stress response to laryngoscopy and intubation. They found that in control group, mean HR was significantly higher than baseline values (30.4% increase) after intubation, and remained higher till ten-minutes post intubation.

We observed that in 1μg/kg group, there was significant increase in mean heart rate from baseline (8.4% increase) immediately after intubation and in patients nebulised with 2μg/kg, there was significant increase in mean heart rate from baseline (4.2% increase) immediately after intubation. This increase lasted till one minute after intubation. In a study conducted by Pranav A Seth et al. [38] it was found that in patients nebulised with 1 μg/kg dexmedetomidine, mean heart rate was significantly higher immediately after intubation than baseline values (4.2% increase) and remained significantly higher till ten-minutes post intubation. However, in our study, 1 μg/kg dexmedetomidine was effective in blunting heart rate response to intubation as compared to baseline.

On inter-group comparison, mean HR remained significantly higher after laryngoscopy and intubation in patients nebulised with normal saline (control group), till ten-minute after intubation as compared to patients nebulised with 1μg/kg and 2μg/kg Dexmedetomidine (p value< 0.05). The mean HR in patients nebulised with 2μg/kg Dexmedetomidine remained comparatively lower as compared to patients nebulised with 1μg/kg Dexmedetomidine throughout the study period but this difference was not statistically significant, indicating that both doses of dexmedetomidine

were almost similar in terms of blunting heart rate response to laryngoscopy and intubation on intergroup comparison.

In a study conducted by Kumar et al. [1] it was found that, there was no significant difference in the HR with nebulisation with dose of 1 μg/kg dexmedetomidine. However, the results from our study showed that nebulised dexmedetomidine 1 μg/kg helped in statistically significant attenuation of rise in heart rate following laryngoscopy and intubation.

SYSTOLIC BLOOD PRESSURE (SBP)

In our study, baseline mean SBP was comparable among three groups ($p>0.05$). In patients nebulised with normal saline (Control group), mean SBP increased significantly from baseline, (121.62 ± 12 to 136.07 ± 9.66 mmHg i.e., 11.8% increase) immediately after intubation and remained significantly higher till five-minutes post intubation. Pranav A Seth et al. [38] conducted a study to evaluate the effect of 1μg/kg dexmedetomidine in comparison to control group (normal saline) by nebulisation for blunting stress response to laryngoscopy and intubation. They found that in control group, mean SBP was higher than baseline values (13.27% increase) after intubation and remained higher till ten-minutes post intubation.

In patients nebulised with 1μg/kg dexmedetomidine, mean SBP increased significantly (from 124.51±9.29 to 128.51±7.83 i.e., 3.2% increase) immediately after intubation from baseline and remained significantly higher till just one minute post intubation. In patients nebulised with 2μg/kg dexmedetomidine, mean SBP immediately after intubation was nearly same as baseline (124.15±10.34 to 123.91±9.09 i.e., 0.91% decrease). Better systolic pressor response control was observed with 2μg/kg dexmedetomidine nebulisation (0.91% decrease) than 1 μg/kg dexmedetomidine nebulisation (3.2% increase) as compared to control group (11.8% increase). In a study conducted by Pranav A Seth et al. [38] it was found that in patient nebulised with 1 μg/kg dexmedetomidine, mean

SBP was nearly same as baseline (114.8 10.73 to 114.88 12.65 i.e., 0.06% increase). Better systolic pressor response control in above study could be because of fixed higher dose (2-2.5mg/kg) of induction agent (Propofol) used as compared to titrable dose of propofol used (mean propofol dose of 1.54 mg/kg in 1 µg/kg dexmedetomidine group) in our study.

Mumtaz et al. [35] conducted a study to evaluate the effect of 2µg/kg dexmedetomidine nebulisation on attenuation of haemodynamic response to laryngoscopy. In patients nebulised with normal saline (Control group), mean SBP increased after intubation from baseline value with highest value at two-minutes post intubation (14.5% increase) from baseline and never reached baseline throughout the study period of 5minutes. In patients nebulised with 2µg/kg dexmedetomidine, mean SBP increased (10.9% increase) immediately after intubation from baseline value and returned to near the baseline value by three-minutes. Their study was limited to five-minutes post intubation.

In our study, on inter-group comparison, mean SBP remained significantly higher immediately after laryngoscopy and intubation in patients nebulised with normal saline, till ten minutes after intubation as compared to patients nebulised with 1µg/kg and 2µg/kg Dexmedetomidine (p value< 0.05). In a study conducted by Kumar et al. [1] it was found that SBP immediately after intubation were comparable in nebulised dexmedetomidine (1µg/kg) and control group (normal saline). The SBP at one, five and ten-minute post intubation were significantly lower in dexmedetomidine group as compared to control group.

In our study the mean SBP in patients nebulised with 2µg/kg Dexmedetomidine remained statistically lower as compared to patients nebulised with 1µg/kg Dexmedetomidine, immediately after intubation till four-minute post intubation. Thus, on intragroup comparison, 2µg/kg Dexmedetomidine more effectively blunted systolic pressor response in comparison to 1µg/kg Dexmedetomidine.

Misra et al. [10] concluded from their study that a single dose of nebulised dexmedetomidine at 1μg/kg, administered 30 min before induction of anesthesia, did not attenuate SBP pressor response after laryngoscopy. In contrast, the results of our study showed significant attenuation of SBP following laryngoscopy and intubation in dexmedetomidine group as compared to control group.

DIASTOLIC BLOOD PRESSURE

In our study, baseline mean DBP were comparable among three groups ($p>0.05$). In control group mean DBP was significantly higher immediately after intubation than baseline values (12.84% increase) and remained significantly higher till three-minutes post intubation. Pranav A Seth et al. [38] in their study found that in control group, mean DBP was significantly higher than baseline values (15.8% increase) after intubation, and remained higher till ten-minutes post intubation.

In patients nebulised with 1μg/kg dexmedetomidine, mean DBP significantly increased (73.25±9.11 to 75.35±10.02 i.e., 2.8% increase) immediately after intubation from baseline, and thereafter mean DBP started decreasing. In patients nebulised with 2μg/kg Dexmedetomidine, although mean DBP increased immediately (73.38±9.46 to 75.36±8.68 i.e., 2.69% increase) after intubation from baseline but it was not statistically significant. Thus, in our study, on intragroup comparison, both doses of dexmedetomidine were found to be effective in attenuation of rise in DBP following laryngoscopy and intubation. In a study conducted by Pranav A Seth et al. [38] it was found that in patient nebulised with 1 μg/kg dexmedetomidine, mean DBP remained lower than baseline throughout the study. In a study conducted by Mumtaz et al. [35] it was found that mean DBP increased (15.19% increase) after intubation from baseline and was back to near the baseline values by three-minutes in patients nebulised with 2μg/kg dexmedetomidine.

In our study, on inter-group comparison, mean DBP remained significantly higher immediately after laryngoscopy and intubation in patients nebulised with normal saline (control group), till nine-minutes after intubation as compared to patients nebulised with 1µg/kg and 2µg/kg Dexmedetomidine (p value< 0.05). In a study conducted by Kumar et al. [1] it was found that DBP immediately after intubation were comparable in nebulised dexmedetomidine (1µg/kg) and control group (normal saline). The reduction in the DBP following laryngoscopy and intubation at one, five and ten-minute were significantly more in dexmedetomidine group as compared to control group. In a study conducted by Mumtaz et al. [35] it was found that the DBP remained significantly higher till three-minutes post intubation in patients nebulised with normal saline as compared to patients nebulised with 2µg/kg dexmedetomidine.

In our study, the mean DBP in 1µg/kg and 2µg/kg Dexmedetomidine groups, immediately after laryngoscopy and intubation, till ten minutes after intubation were comparable (p>0.05). Thus, on intergroup comparison, both doses of 1µg/kg and 2µg/kg Dexmedetomidine were found to be equally effective in blunting DBP response to intubation.

MEAN ARTERIAL PRESSURE

In our study, baseline MAP was comparable among three groups (p>0.05). In control group MAP was significantly higher immediately after intubation than baseline values (12.4% increase) and remained significantly higher till three-minutes post intubation. Pranav A Seth et al. [38] in their study found that in control group, MAP was significantly higher than baseline values (14.7% increase) after intubation, and remained higher till ten-minutes post intubation.

In our study, in patients nebulised with 1µg/kg dexmedetomidine, MAP significantly increased immediately after intubation from baseline, (90.34±8.10 to 93.07±8.28 i.e., 8.28% increase) and thereafter MAP started decreasing. In patients nebulised with 2µg/kg Dexmedetomidine,

although MAP increased (90.30±8.20 to 91.55±7.60 i.e., 1.38% increase) immediately after intubation from baseline but it was not significant. Better MAP pressor response control was observed with 2μg/kg dexmedetomidine nebulisation (1.38% increase) than 1 μg/kg dexmedetomidine nebulisation (8.28% increase) as compared to control group (12.4% increase). In a study conducted by Pranav A Seth et al. [38] it was found that in patient nebulised with 1 μg/kg dexmedetomidine, MAP was nearly same as baseline after intubation. Better MAP pressor response control in above study could be because of fixed higher dose (2-2.5mg/kg) of induction agent (Propofol) used as compared to titrable dose of propofol used (mean propofol dose of 1.54 mg/kg in 1 μg/kg dexmedetomidine group) in our study.

In our study, on inter-group comparison, MAP remained significantly higher immediately after laryngoscopy and intubation in patients nebulised with normal saline, till ten-minutes after intubation as compared to patients nebulised with 1μg/kg and 2μg/kg Dexmedetomidine (p value< 0.05). In a study conducted by Kumar et al. [1] it was found that MAP immediately after intubation were comparable in nebulised dexmedetomidine (1μg/kg) and control group (normal saline). The reduction in the MAP after intubation at one, five and ten-minute were significantly higher in dexmedetomidine group as compared to control group. In a study conducted by Pranav A Seth et al. [38] it was found that in patient nebulised with 1 μg/kg dexmedetomidine, MAP was significantly lower at one minute post intubation as compared to control group (normal saline) and remain significantly lower throughout the study period of ten-minutes.

Mumtaz et al. [35] in their study, found that MAP in patients nebulised with 2μg/kg dexmedetomidine was comparable with patients nebulised with normal saline at one minute post intubation. MAP was significantly lower at two-minute post intubation in patients nebulised with 2μg/kg dexmedetomidine as compared to control group.

In our study, the MAP immediately after laryngoscopy and intubation, till ten minutes after intubation were comparable in 1µg/kg and 2µg/kg Dexmedetomidine groups ($p>0.05$). Thus, on intergroup comparison, both doses of 1µg/kg and 2µg/kg Dexmedetomidine were found to be equally effective in blunting MAP response to intubation

SpO_2

There was no significant difference in SpO_2 in all three groups before nebulisation. All three were comparable with respect to $SpO_{2:}$

Requirement of induction dose of Propofol

Requirement of propofol for induction in control group (normal saline) was 8.4% higher as compared to 1µg/kg group and 19.7% more as compared to patients in 2µg/kg group. Total amount of propofol used in control group, 1µg/kg group and 2µg/kg group were 118.91±26.50 mg (mean value 1.76mg/kg), 108.91± 23.93 mg (mean value 1.54mg/kg) and 95.4 ±18.94 mg (mean value 1.37mg/kg), respectively. Requirement of propofol in 2µg/kg dexmedetomidine patients was 12.3% less as compared to 1µg/kg dexmedetomidine patients. Thus, 2µg/kg dexmedetomidine nebulisation was more effective in reduction of requirement of induction dose of propofol.

A similar reduction in induction dose of propofol was also observed in a study conducted by Satyajeet Misra et al. [10] using 1µg/kg dexmedetomidine nebulisation as compared to control group.

TIME OF INTUBATION

All the three groups were comparable with respect to time of intubation. There was no statistically significant difference.

SIDE EFFECTS

In our study, both doses of 1µg/kg and 2µg/kg Dexmedetomidine were not associated with any significant side effects like bradycardia, tachycardia,

hypotension, or hypertension, requiring any intervention. Pranav et al. [37] in their study, also found that 1µg/kg nebulised dexmedetomidine was not associated with any of adverse effects. In a study conducted by Mumtaz et al. [35] no adverse effects like bradycardia or hypotension were seen in patients nebulised with 2µg/kg Dexmedetomidine.

There are certain limitations to our study: Cases with difficult airway were excluded, which may be associated with more pressor response and hence we could not study the beneficial effect of 1µg/kg and 2µg/kg Dexmedetomidine nebulisation in these special scenarios. Similarly, the results cannot be extrapolated to high-risk patients with comorbidities, as they were excluded from the study protocol.

SUMMARY AND CONCLUSION

The present study was conducted in the Department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana after getting approval from the institutional ethical committee. The aim of the study was to compare pre-operative nebulisation with 1 and 2μg/kg of dexmedetomidine in blunting haemodynamic response to laryngoscopy and intubation.

A total number of 165 patients belonging to ASA I and II grade, scheduled for an elective surgery under general anaesthesia were studied in a prospective, randomized, clinical trial after obtaining a written informed consent. Patients were randomly allocated into three groups of 55 patients each using computer generated random numbers.

Group 0: Patients were nebulised with 5 ml of solution containing 0.9% sodium chloride (NaCl)

Group I: Patients were nebulised with 5 ml of solution containing 1μg/kg of dexmedetomidine in 0.9% NaCl.

Group II: Patients were nebulised with 5 ml of solution containing 2μg/kg of dexmedetomidine in 0.9% NaCl.

The patients were nebulised preoperatively for ten-minutes with allocated study drug, ten-minutes before induction of general anesthesia and endotracheal intubation done by experienced anaesthesiologist. Haemodynamic parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (SpO2) were recorded till ten -minutes post intubation.

We observed 1) Both 1μg/kg and 2μg/kg nebulised dexmedetomidine were almost similar in terms of blunting heart rate response to laryngoscopy and intubation.

2) Better systolic pressor response control was observed with 2μg/kg dexmedetomidine nebulisation as compared to 1 μg/kg dexmedetomidine nebulization

3) Both 1µg/kg and 2µg/kg nebulised dexmedetomidine were found to be equally effective in blunting DBP response to laryngoscopy and intubation.

4) Both 1µg/kg and 2µg/kg nebulised dexmedetomidine were found to blunt MAP response to laryngoscopy and intubation but 2µg/kg nebulised dexmedetomidine was more effective in blunting the MAP response to laryngoscopy and intubation than 1µg/kg nebulised dexmedetomidine

5) The requirement of induction dose of propofol was lesser in 2µg/kg nebulised dexmedetomidine group than 1µg/kg nebulised dexmedetomidine group.

6) Both 1µg/kg and 2µg/kg nebulised Dexmedetomidine were not associated with any significant side effects, requiring any intervention.

Hence, we conclude that, although pre-operative nebulisation with both 1µg/kg and 2µg/kg dexmedetomidine helps to blunt haemodynamic response to laryngoscopy and intubation, nebulisation with 2µg/kg dexmedetomidine appears to be more effective than nebulisation with 1µg/kg dexmedetomidine in terms of better control of the blood pressure pressor response.

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KEYS TO MASTER CHART

ASA	American Society of Anesthesiologists
BMI	Body mass index
cm	Centimeter
DBP	Diastolic blood pressure
HTN	Hypertension
HR	Heart rate
Kg	Kilograms
kg/m^2	Kilograms per meter square
m	Meter
MAP	Mean arterial pressure
min	Minutes
MRD no	Medical records department number
secs	Seconds
S. No	Serial number
SBP	Systolic blood pressure
SpO2	Oxygen saturation

Serial No.	Study Code	Study Group	Name	Age	Sex	MRD no.	Height (cm)	height (m)	Weight(Kg)	BMI (Kg/m2)	ASA grade	Mallam pati class	Thyrome ntral distance	Comorbidities	Induction dose of propofol (mg)	Cormack lehane classification	Time of intubation(se cs)	Heart Rate_Before nebulisation	Heart Rate_During Nebulisation 5 min	Heart Rate_During Nebulisation 10 min	Heart Rate_After Nebulisation 5th min	Heart Rate_After Nebulisation 10th min	Heart Rate_Just before intubation	Heart Rate_Immediately after intubation
1	A	2	K	23	M	1126428	170	1.7	95	32.9	I	2	>6.5cm	No	120	2a	14	90	92	94	90	95	91	100
2	B	2	HS	20	M	1133818	173	1.73	65	21.7	I	1	>6.5cm	No	80	2a	16	79	77	75	74	80	68	80
3	C	0	GG	23	F	956700	160	1.6	58	22.7	I	1	>6.5cm	No	100	1	15	80	82	80	81	80	70	120
4	D	1	P	29	M	912696	157	1.57	58	23.5	I	1	>6.5cm	No	90	1	15	110	100	98	100	93	87	104
5	E	0	K	25	F	1126191	157	1.57	40	16.2	I	1	>6.5cm	No	100	1	16	82	80	82	83	80	83	98
6	F	2	R	64	M	1126049	167	1.67	80	28.7	I	2	>6.5cm	No	80	1	15	83	80	85	78	79	80	84
7	G	2	J	17	M	1128297	175	1.75	60	19.6	I	1	>6.5cm	No	80	1	14	90	84	85	86	84	80	94
8	H	2	K	25	F	1126191	157	1.57	40	16.2	I	2	>6.5cm	No	80	1	15	82	80	88	80	84	87	98
9	I	1	A	28	M	1105172	175	1.75	100	32.7	I	2	>6.5cm	No	150	1	14	90	85	84	80	75	78	87
10	J	1	R	51	M	1332894	162	1.62	60	22.9	I	2	>6.5cm	No	120	2a	15	85	86	84	87	85	72	88
11	K	2	S	35	M	1129901	160	1.6	70	27.3	I	1	>6.5cm	No	90	2a	13	88	80	85	84	84	75	88
12	L	0	S	43	F	1128798	163	1.63	75	28.2	II	2	>6.5cm	HTN	100	2a	13	90	90	89	92	93	90	115
13	M	2	K	38	F	1122661	157	1.57	61	24.7	I	1	>6.5cm	No	100	1	14	90	88	88	85	88	84	98
14	N	2	J	36	M	999902	175	1.75	64	20.9	II	2	>6.5cm	Hypothyroid	80	2a	15	67	62	64	62	64	63	60
15	O	0	V	50	F	1131067	160	1.6	75	29.3	I	2	>6.5cm	No	100	2a	14	89	87	88	87	82	90	89
16	P	1	MG	39	F	1130993	152	1.52	80	34.6	I	1	>6.5cm	No	100	1	14	80	84	82	83	85	83	88
17	Q	2	KC	43	M	905506	168	1.68	65	23.0	I	1	>6.5cm	No	100	2a	15	70	68	67	67	67	60	70
18	R	0	R	39	F	7813	163	1.63	90	33.9	II	2	>6.5cm	Hypothyroid	140	2a	15	91	90	87	91	99	98	117
19	S	0	RG	38	F	330425	160	1.6	65	25.4	I	1	>6.5cm	No	120	1	14	99	98	97	97	96	92	120
20	T	1	S	22	F	1132119	163	1.63	75	28.2	I	1	>6.5cm	No	70	1	15	80	85	84	90	86	70	99
21	U	0	SS	27	M	979559	163	1.63	75	28.2	I	1	>6.5cm	No	80	1	12	106	105	103	102	104	100	117
22	V	2	D	45	M	1129640	170	1.7	90	31.1	I	2	>6.5cm	No	100	2a	13	78	78	77	74	75	75	84
23	W	2	P	58	F	1131658	160	1.6	80	31.3	I	2	>6.5cm	No	90	2a	15	79	78	78	77	78	75	82
24	X	2	DR	33	F	113338	152	1.52	55	23.8	I	1	>6.5cm	No	80	1	15	67	69	70	70	70	65	80
25	Y	2	N	31	M	285255	170	1.7	80	27.7	I	1	>6.5cm	No	100	2a	14	54	53	52	51	51	50	72
26	Z	2	A	24	F	1003129	168	1.68	60	21.3	I	1	>6.5cm	No	80	1	12	89	86	85	85	85	84	92
27	AA	1	S	43	F	1139328	147	1.47	60	27.8	I	1	>6.5cm	No	80	1	12	89	88	88	85	84	82	90
28	AB	1	G	43	F	1138867	157	1.57	72	29.2	I	2	>6.5cm	No	110	2a	16	65	64	63	64	62	60	74
29	AC	1	SK	32	F	1140151	168	1.68	50	17.7	I	1	>6.5cm	No	80	1	12	90	90	89	90	89	85	95
30	AD	1	N	36	M	835205	160	1.6	65	25.4	I	1	>6.5cm	No	90	2a	16	98	97	95	95	93	85	95
31	AE	2	PK	35	F	1149136	160	1.6	72	28.1	I	2	>6.5cm	No	120	2a	14	90	85	80	84	83	68	94
32	AF	1	L	29	M	1168218	168	1.68	80	28.3	I	1	>6.5cm	No	130	2a	15	72	71	72	70	68	62	74
33	AG	1	M	30	M	1163988	165	1.65	75	27.5	I	2	>6.5cm	No	100	2a	12	83	82	80	79	79	71	76
34	AH	0	G	37	M	267496	162	1.62	60	22.9	I	2	>6.5cm	No	120	2a	14	83	82	85	84	83	70	100
35	AI	1	R	39	M	1125191	162	1.62	75	28.6	I	2	>6.5cm	No	120	2a	14	89	88	85	84	82	70	92
36	AJ	1	H	58	M	1168030	170	1.7	74	25.6	I	2	>6.5cm	No	100	2a	14	80	78	75	76	74	69	78
37	AK	1	KM	60	F	1169912	160	1.6	68	26.6	I	2	>6.5cm	No	120	2a	15	72	72	71	71	70	68	89
38	AL	0	MS	59	M	1169044	170	1.7	60	20.8	I	2	>6.5cm	No	100	2a	14	55	55	56	54	52	52	79
39	AM	1	DR	50	M	1212875	178	1.78	85	26.8	II	2	>6.5cm	HTN	100	2a	15	56	55	56	56	56	55	60
40	AN	0	M	20	M	507041	162	1.62	70	26.7	I	1	>6.5cm	No	200	1	16	62	62	60	62	60	58	110
41	AO	2	A	27	M	612325	170	1.7	70	24.2	I	2	>6.5cm	No	80	2a	15	84	83	83	84	83	80	90
42	AP	1	H	23	M	1175775	178	1.78	70	22.1	I	1	>6.5cm	No	100	1	15	88	85	84	86	87	80	103
43	AQ	0	S	32	M	1175657	168	1.68	75	26.6	I	2	>6.5cm	No	120	2a	16	79	80	79	78	79	68	90
44	AR	2	A	45	F	1177046	162	1.62	60	22.9	I	2	>6.5cm	No	80	2a	12	80	82	84	84	84	89	90
45	AS	1	R	34	F	118010	160	1.6	50	19.5	I	2	>6.5cm	No	100	2a	14	80	79	80	80	75	75	88
46	AT	1	R	40	F	1177607	167	1.67	88	31.6	I	1	>6.5cm	No	100	1	15	66	64	64	64	64	65	80
47	AU	0	A	32	M	1179662	185	1.85	100	29.2	I	1	>6.5cm	No	200	2b	14	85	85	88	86	87	80	105
48	AV	1	GK	30	F	742376	163	1.63	65	24.5	I	1	>6.5cm	No	100	2a	15	88	87	88	89	88	80	95
49	AW	0	RK	27	M	1197589	165	1.65	62	22.8	I	1	>6.5cm	No	100	1	13	79	78	79	80	78	70	100
50	AX	1	BK	53	F	1189874	165	1.65	50	18.4	I	2	>6.5cm	No	80	2a	15	65	66	65	66	64	60	70
51	AY	2	P	28	F	296368	160	1.6	65	25.4	I	2	>6.5cm	No	80	1	15	94	92	93	89	88	73	94
52	AZ	1	B	34	M	1192931	163	1.63	65	24.5	I	1	>6.5cm	No	100	2a	15	89	88	85	83	80	73	94
53	BA	0	R	36	M	654266	170	1.7	70	24.2	I	2	>6.5cm	No	120	2a	15	93	93	95	96	94	89	115
54	BB	0	VK	45	F	1218983	160	1.6	55	21.5	I	2	>6.5cm	No	80	1	16	74	72	75	72	70	65	100
55	BC	2	RS	39	M	567942	152	1.52	70	30.3	I	2	>6.5cm	No	80	2a	12	92	92	90	88	88	80	95
56	BD	0	A	19	F	1205017	160	1.6	50	19.5	I	2	>6.5cm	No	100	2a	13	84	85	84	86	85	78	98
57	BE	0	P	38	M	1179607	175	1.75	100	32.7	II	2	>6.5cm	No	100	1	14	99	98	95	95	96	90	100
58	BF	0	A	27	F	1173672	157	1.57	63	25.6	I	2	>6.5cm	No	100	2a	15	80	80	80	78	80	78	99
59	BG	1	J	46	M	1213527	170	1.7	80	27.7	I	1	>6.5cm	No	100	2a	15	98	98	97	95	97	88	109
60	BH	1	M	51	F	326323	165	1.65	75	27.5	II	2	>6.5cm	Hypothyroid	100	2a	15	84	83	82	83	80	70	95
61	BI	1	H	24	F	1216460	160	1.6	60	23.4	I	2	>6.5cm	No	80	2a	14	80	79	80	78	82	75	88
62	BJ	0	H	43	F	424510	165	1.65	65	23.9	I	2	>6.5cm	No	90	2a	16	90	90	92	90	89	80	100
63	BK	0	RS	40	M	1218932	180	1.8	75	23.1	I	2	>6.5cm	No	120	1	12	58	57	57	59	58	55	72

Serial No.	Study Code	Heart Rate_1 min	Heart Rate_2 min	Heart Rate_3 min	Heart Rate_4 min	Heart Rate_5 min	Heart Rate_6 min	Heart Rate_7 min	Heart Rate_8 min	Heart Rate_9 min	Heart Rate_10 min	SpO2_Before nebulisation	SpO2_During Nebulisation 5 min	SpO2_During Nebulisation 10 min	SpO2_After Nebulisation 5th min	SpO2_After Nebulisation 10th min	SpO2_Just before intubation	SpO2_Immediately after intubation	SpO2_1 min	SpO2_2 min	SpO2_3 min
1	A	96	97	95	92	89	90	82	80	77	86	99	99	99	99	100	100	99	99	100	100
2	B	78	80	79	75	73	72	70	69	67	65	99	99	100	100	100	100	100	99	100	100
3	C	118	117	119	116	112	110	106	102	100	98	100	100	99	100	100	100	100	100	100	99
4	D	97	70	72	80	84	84	80	87	84	80	100	100	100	100	99	100	99	100	100	100
5	E	100	96	100	98	97	96	95	90	89	87	98	99	99	100	99	100	99	100	100	99
6	F	82	80	74	75	75	76	74	74	76	75	100	100	100	100	100	100	100	100	100	100
7	G	89	88	88	84	82	84	80	84	80	80	99	99	99	100	100	100	100	100	100	100
8	H	98	100	92	98	94	92	92	91	90	90	98	99	99	99	99	99	100	100	100	100
9	I	86	84	86	84	83	84	88	85	84	82	98	99	98	99	99	100	100	100	100	100
10	J	87	88	86	87	85	85	86	85	84	83	100	100	100	100	100	100	100	100	100	100
11	K	87	85	85	80	80	79	75	70	68	65	99	100	100	100	100	100	100	100	100	100
12	L	115	110	99	98	98	97	96	97	96	95	100	100	100	100	100	100	100	100	100	100
13	M	85	85	84	83	85	80	82	82	84	84	98	99	98	99	99	99	99	99	99	99
14	N	64	63	64	58	60	64	65	66	64	60	100	100	100	100	100	100	100	100	100	100
15	O	84	90	92	94	88	86	84	87	83	84	100	100	100	100	100	100	100	100	100	100
16	P	87	87	86	85	86	85	85	84	84	83	100	100	100	100	100	100	100	100	100	100
17	Q	74	73	71	73	71	74	73	72	68	69	100	100	100	100	100	100	100	100	100	100
18	R	116	114	112	110	108	106	100	98	96	94	99	100	100	100	100	100	100	100	100	100
19	S	120	118	117	116	115	114	109	109	105	104	100	100	100	100	100	100	100	100	100	100
20	T	89	85	84	84	84	83	80	78	75	75	99	99	100	99	100	100	100	100	100	100
21	U	118	124	123	120	120	120	118	116	110	110	97	98	97	98	98	100	100	100	100	100
22	V	80	80	79	78	79	79	78	79	79	79	99	99	99	98	99	99	99	100	100	100
23	W	80	80	79	80	78	75	74	73	74	76	98	98	98	99	98	98	100	100	100	100
24	X	79	82	80	84	82	80	78	76	77	79	98	97	98	98	99	100	100	99	99	100
25	Y	70	68	65	66	67	68	65	64	62	60	98	98	99	98	98	100	99	100	100	100
26	Z	90	90	78	78	79	77	76	75	76	75	100	100	100	99	100	100	100	100	100	100
27	AA	76	72	73	72	72	80	74	72	69	64	99	99	99	100	100	100	100	100	100	100
28	AB	73	70	69	72	68	65	64	63	61	60	100	100	100	98	100	100	100	100	100	100
29	AC	94	92	90	90	88	86	85	84	82	80	100	100	100	100	100	100	100	100	100	100
30	AD	93	90	86	84	80	79	78	77	80	82	99	100	100	100	100	100	100	100	100	100
31	AE	97	91	90	90	91	88	85	86	85	84	100	100	100	100	100	100	100	100	100	100
32	AF	73	72	74	72	73	70	68	69	70	68	99	99	99	99	98	99	100	99	99	99
33	AG	77	73	71	71	69	68	67	68	68	69	99	100	100	100	100	100	100	100	100	100
34	AH	98	97	95	93	95	96	97	92	90	88	100	99	100	100	99	100	100	100	99	99
35	AI	90	85	82	84	83	89	80	78	75	73	100	99	100	100	100	99	100	100	100	100
36	AJ	75	70	72	75	74	70	69	65	68	63	100	100	99	100	99	100	100	100	99	100
37	AK	86	84	82	82	82	80	80	78	75	74	99	99	99	100	99	100	100	100	100	100
38	AL	78	77	75	74	72	74	70	68	65	62	99	99	100	99	99	99	100	99	100	100
39	AM	59	60	59	60	58	55	55	55	54	55	100	100	100	100	100	100	100	100	100	100
40	AN	95	93	92	92	90	90	90	88	88	87	98	98	98	99	99	99	99	98	99	99
41	AO	90	89	88	89	88	88	87	85	84	84	100	100	100	100	100	100	100	99	100	100
42	AP	93	94	90	90	88	85	82	86	79	78	100	100	99	100	100	100	99	100	100	100
43	AQ	78	77	76	77	72	77	79	78	77	72	100	100	100	100	100	100	100	100	100	100
44	AR	89	84	78	78	74	72	73	78	74	72	100	100	100	100	100	100	100	100	100	100
45	AS	88	85	80	80	80	79	79	80	79	78	100	100	100	100	100	100	100	100	100	100
46	AT	66	63	63	64	62	62	62	62	63	64	100	100	100	100	100	100	100	100	100	100
47	AU	100	100	101	98	97	95	93	88	87	85	99	100	100	99	100	100	100	100	100	100
48	AV	92	94	90	90	89	85	84	82	80	80	99	99	99	99	99	99	99	100	100	100
49	AW	99	100	95	93	90	88	87	88	86	85	100	100	100	100	100	100	100	100	100	100
50	AX	70	72	73	72	70	68	67	69	67	65	100	100	98	100	100	100	100	99	100	99
51	AY	92	90	89	91	92	85	88	84	83	81	100	100	100	100	100	100	100	100	100	100
52	AZ	92	89	93	85	79	80	82	81	78	75	99	99	100	99	100	99	99	99	98	99
53	BA	114	115	110	108	105	104	102	100	98	93	99	99	98	99	99	100	99	99	100	99
54	BB	98	97	98	96	94	92	90	90	88	85	100	100	100	100	100	100	100	100	100	100
55	BC	93	93	91	89	89	90	89	88	89	88	100	100	100	100	100	100	100	100	100	100
56	BD	95	94	96	98	90	89	87	88	85	84	100	99	100	99	99	100	100	100	100	100
57	BE	99	99	98	95	93	92	90	90	89	88	99	99	98	99	100	99	99	99	99	100
58	BF	98	98	100	97	95	80	80	79	79	80	100	100	100	100	100	100	100	100	100	100
59	BG	104	105	105	104	95	95	94	95	93	92	100	100	100	100	100	100	100	100	100	100
60	BH	93	92	94	94	93	90	88	89	90	89	100	100	100	100	100	100	100	100	100	100
61	BI	86	87	85	82	80	78	78	77	76	77	100	100	100	100	100	100	100	100	100	100
62	BJ	99	97	98	97	95	93	92	90	88	85	99	98	99	99	98	100	100	99	99	100
63	BK	70	68	65	64	62	65	64	63	62	61	100	100	100	99	100	100	100	100	100	100

Serial No.	Study Code	SpO2_4 min	SpO2_5 min	SpO2_6 min	SpO2_7 min	SpO2_8 min	SpO2_9 min	SpO2_10 min	SBP_Before nebulisation	SBP_During Nebulisation 5 min	SBP_During Nebulisation 10 min	SBP_After Nebulisation 5th min	SBP_After Nebulisation 10th min	SBP_Just before intubation	SBP_Immediately after intubation	SBP_1 min	SBP_2 min	SBP_3 min	SBP_4 min	SBP_5 min	SBP_6 min	SBP_7 min	SBP_8 min	SBP_9 min	SBP_10 min
1	A	99	99	98	99	99	99	99	118	120	120	124	125	117	148	137	133	125	125	122	132	123	122	122	118
2	B	99	100	99	100	100	99	100	116	116	115	117	116	100	120	120	118	116	117	118	114	119	112	102	100
3	C	100	100	98	100	100	100	100	100	100	99	100	99	90	130	129	127	120	126	120	118	116	112	111	110
4	D	100	100	100	100	100	100	100	136	130	130	130	128	109	145	130	120	123	119	111	112	109	113	115	129
5	E	100	99	99	99	99	99	99	130	120	129	129	110	93	114	115	108	109	100	102	100	101	98	98	97
6	F	100	100	100	100	100	100	100	138	130	120	129	120	130	120	122	120	115	120	118	115	116	120	121	120
7	G	100	100	100	100	100	100	100	133	137	130	127	126	107	155	149	136	122	131	125	132	136	101	122	117
8	H	100	100	100	100	100	100	100	128	129	130	123	120	101	125	101	103	109	108	115	114	110	112	116	116
9	I	100	100	100	100	100	100	100	140	129	130	122	121	114	140	130	125	114	115	114	114	120	112	115	112
10	J	100	100	100	100	100	100	100	132	130	128	130	125	110	125	125	122	124	125	124	120	120	118	115	118
11	K	99	100	99	100	100	100	100	136	137	138	112	102	100	120	125	114	112	110	111	110	108	105	102	105
12	L	100	100	100	100	100	100	100	160	152	152	160	150	130	165	150	152	149	148	145	138	135	132	132	135
13	M	99	99	99	99	99	99	99	142	142	140	138	114	106	130	120	122	122	120	117	120	120	116	117	110
14	N	100	100	100	100	100	100	100	158	163	160	150	155	132	135	130	136	129	134	133	125	128	123	132	126
15	O	100	100	100	100	100	100	100	120	120	118	112	97	92	140	139	135	139	123	128	125	118	122	124	120
16	P	100	100	100	100	100	100	100	138	135	130	129	129	126	136	113	117	107	110	109	111	108	110	123	115
17	Q	100	100	100	100	100	100	100	127	129	129	129	124	113	130	125	116	115	110	113	115	112	110	114	114
18	R	100	100	100	100	100	100	100	108	108	120	129	109	104	142	141	140	138	135	125	124	120	112	116	118
19	S	100	100	100	100	100	100	100	130	128	125	124	120	118	155	150	149	140	135	130	124	124	122	118	118
20	T	100	100	100	100	100	100	100	139	137	135	137	125	105	133	124	125	124	120	118	115	114	112	108	110
21	U	100	100	100	100	100	100	100	110	120	124	120	117	124	134	128	123	127	126	118	116	114	112	110	104
22	V	99	100	99	100	100	100	100	120	115	114	106	109	107	120	120	117	116	113	112	112	114	117	116	115
23	W	99	100	99	100	100	100	100	148	146	147	135	133	125	140	135	134	128	125	125	126	127	125	128	125
24	X	99	100	99	100	100	100	100	118	120	118	122	116	98	120	120	122	120	116	117	118	116	117	114	114
25	Y	98	100	99	99	99	99	99	114	115	103	117	112	100	119	118	117	116	115	118	115	109	105	115	109
26	Z	99	99	100	99	100	100	100	118	118	110	113	111	96	126	117	127	118	103	102	100	103	101	104	94
27	AA	100	100	100	100	100	100	100	120	120	119	115	119	92	122	102	100	97	93	93	96	91	98	95	90
28	AB	100	100	100	100	100	100	100	130	126	124	120	118	110	130	129	128	125	122	118	117	115	112	108	110
29	AC	100	100	100	100	100	100	100	130	129	120	124	120	116	128	126	125	130	124	122	120	118	116	120	117
30	AD	99	99	100	100	100	100	100	125	124	120	118	120	112	129	128	124	118	119	118	120	118	113	109	110
31	AE	100	100	100	100	100	100	100	147	130	128	117	118	112	121	119	118	118	116	115	118	119	115	118	117
32	AF	100	100	100	99	99	99	99	120	118	115	118	116	110	129	128	126	125	124	120	118	120	118	119	116
33	AG	100	100	100	100	100	100	100	130	128	125	124	120	92	121	115	108	100	105	111	104	109	110	112	113
34	AH	99	99	98	99	100	99	99	123	125	124	119	126	102	129	126	118	120	113	122	109	105	118	102	105
35	AI	100	100	100	100	100	100	100	119	118	120	118	109	102	120	120	118	115	119	120	113	115	109	105	101
36	AJ	100	100	100	100	100	100	100	128	125	119	120	119	108	123	120	122	118	109	113	112	115	109	108	104
37	AK	100	100	100	100	100	100	100	132	132	134	132	130	118	134	132	132	130	130	124	122	120	120	120	118
38	AL	100	100	100	100	100	100	100	100	101	105	102	101	92	130	128	128	126	125	125	124	124	122	120	118
39	AM	100	100	100	100	100	100	100	112	113	118	120	108	109	126	121	124	123	123	120	125	120	125	118	113
40	AN	99	99	98	99	98	99	98	135	136	134	132	130	133	163	148	136	128	124	123	124	125	128	123	122
41	AO	100	100	100	100	100	100	100	128	128	125	127	120	112	125	125	118	115	114	120	113	115	113	114	114
42	AP	100	100	100	100	100	100	100	125	124	123	120	119	107	123	126	116	120	121	118	120	119	121	116	114
43	AQ	100	100	100	100	100	100	100	130	130	128	130	129	102	128	125	126	113	116	120	119	118	116	116	115
44	AR	100	100	100	100	100	100	100	116	117	115	109	109	96	105	104	104	104	102	103	105	104	104	104	101
45	AS	100	100	100	100	100	100	100	120	120	118	118	120	112	129	128	128	125	120	120	118	116	120	119	118
46	AT	100	100	100	100	100	100	100	123	114	115	108	114	114	115	109	87	110	109	98	99	98	104	115	112
47	AU	100	100	100	100	100	100	100	130	125	130	128	130	99	139	137	136	135	132	129	125	124	123	122	120
48	AV	99	99	99	99	99	98	99	110	110	110	108	120	100	120	120	118	120	115	114	114	116	115	112	110
49	AW	100	100	100	100	100	100	100	110	110	112	110	114	98	130	128	125	128	124	120	118	119	118	116	115
50	AX	99	100	100	100	100	100	100	128	125	128	126	125	110	122	121	120	118	120	116	115	114	113	112	110
51	AY	100	100	100	100	100	100	100	121	122	120	121	120	112	125	122	120	118	116	119	110	112	110	111	108
52	AZ	100	100	99	99	99	99	99	120	118	116	115	117	108	128	126	124	120	123	118	115	109	110	112	105
53	BA	98	99	99	99	98	99	99	123	123	122	120	124	112	142	139	140	138	136	139	135	130	129	125	124
54	BB	100	100	100	100	100	100	100	100	100	100	99	100	99	130	128	130	128	126	124	120	120	118	115	110
55	BC	100	100	100	100	100	100	100	126	120	118	114	114	118	120	117	107	105	104	104	104	103	108	109	106
56	BD	99	100	100	100	100	100	100	124	125	124	118	120	108	129	125	120	118	116	115	113	114	109	110	110
57	BE	99	99	99	100	100	100	100	120	120	119	118	119	118	129	128	125	124	122	120	124	120	118	116	114
58	BF	100	100	100	100	100	100	100	100	100	100	99	98	95	120	120	108	101	97	101	101	98	98	98	97
59	BG	100	100	100	100	100	100	100	130	130	128	125	120	98	134	130	128	128	125	124	130	125	125	120	118
60	BH	100	100	100	100	100	100	100	118	117	118	116	110	100	122	120	121	120	119	110	112	110	109	100	99
61	BI	100	100	100	100	100	100	100	99	98	100	100	99	90	110	111	115	114	112	110	112	110	99	100	96
62	BJ	98	99	99	99	99	99	99	118	118	117	119	120	112	129	128	125	118	115	108	110	105	100	102	101
63	BK	100	100	100	100	100	100	100	108	108	105	109	108	100	140	139	138	135	135	134	133	132	130	128	124

Serial No.	Study Code	DBP_Before nebulisation	DBP_During Nebulisation 5 min	DBP_During Nebulisation 10 min	DBP_After Nebulisation 5th min	DBP_After Nebulisation 10th min	DBP_Just before intubation	DBP_Immediately after intubation	DBP_1 min	DBP_2 min	DBP_3 min	DBP_4 min	DBP_5 min	DBP_6 min	DBP_7 min	DBP_8 min	DBP_9 min	DBP_10 min	MAP_Before nebulisation
1	A	77	67	80	88	90	56	85	80	69	66	59	59	60	55	54	54	54	91
2	B	67	67	68	65	63	60	70	68	65	64	63	60	63	60	63	60	59	83
3	C	60	61	62	60	60	55	70	69	68	65	63	62	60	59	61	64	60	73
4	D	96	96	80	90	87	73	95	88	77	68	76	81	79	80	79	65	77	109
5	E	80	80	80	77	70	59	71	65	67	63	62	60	61	63	62	60	60	97
6	F	77	67	70	70	80	80	80	70	75	70	70	70	80	70	80	70	70	97
7	G	76	77	84	84	78	54	101	86	79	69	80	85	75	70	50	68	68	95
8	H	77	74	90	70	79	46	60	46	69	63	67	65	71	74	86	72	83	94
9	I	96	88	86	84	78	67	119	88	80	72	72	75	67	70	72	70	69	111
10	J	70	70	71	68	69	65	72	73	68	66	68	75	70	70	70	68	70	91
11	K	77	87	78	73	65	60	80	79	75	74	70	68	65	64	62	62	60	97
12	L	109	92	94	100	90	70	128	99	98	95	95	90	76	75	78	80	75	126
13	M	92	90	92	90	65	59	90	78	68	69	68	68	65	65	65	68	70	109
14	N	91	83	80	80	78	84	85	80	70	79	80	70	65	80	70	70	65	113
15	O	80	70	68	81	67	69	90	88	87	80	85	82	75	72	69	70	69	93
16	P	76	60	70	89	78	76	81	84	72	66	68	72	70	69	67	65	60	97
17	Q	86	77	79	89	74	74	88	79	76	72	74	68	65	60	60	58	54	100
18	R	68	68	70	77	66	96	91	74	70	65	64	68	67	65	68	66	60	81
19	S	70	68	67	68	65	66	70	68	65	60	62	80	92	91	84	83	79	90
20	T	90	88	90	89	75	57	88	80	78	78	78	78	75	74	68	65	69	106
21	U	70	70	81	79	75	78	97	77	87	88	70	70	68	68	65	64	59	83
22	V	55	62	65	59	63	53	68	65	68	65	68	69	74	75	68	67	70	77
23	W	86	88	84	80	82	78	85	79	78	80	78	78	75	75	78	77	74	107
24	X	65	67	72	68	70	68	70	65	70	64	62	60	64	66	67	68	65	83
25	Y	78	77	82	78	75	65	80	79	78	75	70	68	72	69	68	62	60	90
26	Z	67	69	70	77	75	56	91	73	72	74	52	52	60	52	54	55	52	84
27	AA	70	69	69	65	61	56	78	57	63	53	54	55	54	54	56	56	56	87
28	AB	65	65	63	62	59	55	62	61	59	58	58	58	59	60	60	64	59	87
29	AC	70	70	65	68	70	70	76	72	68	63	66	68	65	64	60	58	60	90
30	AD	79	78	70	69	72	69	76	73	68	67	70	70	69	65	58	61	62	94
31	AE	86	67	68	71	64	58	80	73	72	70	72	73	68	65	70	69	71	106
32	AF	70	68	65	60	65	60	73	73	72	70	68	72	70	69	69	70	69	87
33	AG	85	84	85	82	80	81	83	68	64	60	58	61	63	62	56	55	62	100
34	AH	69	70	68	69	72	60	74	73	70	69	73	68	65	60	59	61	59	87
35	AI	75	75	74	72	70	68	73	72	63	68	61	60	71	70	66	65	63	90
36	AJ	70	68	70	69	73	60	67	66	63	61	68	65	64	60	61	65	66	89
37	AK	75	74	72	70	68	60	78	76	73	72	70	70	68	65	62	62	60	94
38	AL	60	60	62	60	59	50	72	70	68	67	68	65	64	63	62	61	58	73
39	AM	72	73	75	75	80	75	88	79	85	86	84	70	80	70	66	64	73	85
40	AN	74	76	74	74	70	64	97	86	76	71	67	65	65	64	70	66	60	94
41	AO	65	67	68	72	70	72	82	78	64	70	67	70	73	70	74	69	67	86
42	AP	66	65	68	68	69	62	72	52	60	60	61	64	60	62	61	60	59	86
43	AQ	77	75	78	75	74	62	76	76	72	67	62	62	67	65	64	60	62	95
44	AR	74	75	78	91	79	67	72	73	72	80	74	75	70	72	74	72	73	88
45	AS	70	69	70	68	60	60	68	68	63	63	60	62	60	62	60	60	60	87
46	AT	92	71	65	67	71	60	62	64	46	65	58	57	58	61	56	64	64	102
47	AU	70	68	72	69	71	54	78	77	77	70	72	70	68	69	70	68	65	90
48	AV	65	64	65	68	60	64	76	75	76	73	68	68	65	62	58	64	58	80
49	AW	60	62	58	59	55	58	75	74	73	70	72	68	65	60	66	60	58	77
50	AX	75	74	70	68	76	60	66	63	64	63	62	65	64	62	58	60	62	93
51	AY	66	62	62	63	63	59	69	68	65	69	65	59	60	63	62	60	59	84
52	AZ	70	69	70	68	65	65	70	68	66	67	57	60	63	62	57	58	55	87
53	BA	65	66	68	67	63	60	79	78	75	74	72	70	68	70	69	65	63	84
54	BB	65	64	62	68	60	60	70	69	68	65	64	64	64	60	58	56	60	77
55	BC	68	67	68	67	60	63	76	64	59	54	51	53	54	57	67	68	55	87
56	BD	83	82	80	78	81	75	84	83	79	78	75	70	68	63	62	60	65	97
57	BE	70	69	68	70	69	68	72	70	69	68	65	64	70	60	60	59	55	87
58	BF	70	70	69	72	70	54	75	70	64	64	60	54	71	70	70	68	65	80
59	BG	70	68	70	68	70	60	92	90	92	92	91	94	90	80	76	70	64	90
60	BH	69	68	65	64	65	60	68	67	66	63	62	68	63	65	61	60	60	85
61	BI	60	59	58	55	59	50	63	62	66	58	58	62	58	55	53	60	52	73
62	BJ	59	60	59	63	60	55	69	65	64	62	60	59	63	61	59	61	58	79
63	BK	65	66	65	64	63	58	78	78	78	75	74	72	74	70	68	65	62	79

Serial No.	Study Code	MAP_During Nebulisation 5 min	MAP_During Nebulisation 10 min	MAP_After Nebulisation 5th min	MAP_After Nebulisation 10th min	MAP_Just before intubation	MAP_Immediately after intubation	MAP_1 min	MAP_2 min	MAP_3 min	MAP_4 min	MAP_5 min	MAP_6 min	MAP_7 min	MAP_8 min	MAP_9 min	MAP_10 min	Adverse event	Treatment given
1	A	85	93	100	102	76	106	99	90	86	81	80	84	78	77	77	75		
2	B	83	84	82	81	73	87	85	83	81	81	79	80	80	79	74	73		
3	C	74	74	73	73	67	90	89	88	83	84	81	79	78	78	80	77		
4	D	107	97	103	101	85	112	102	91	86	90	91	90	90	90	82	94		
5	E	93	96	94	83	70	85	82	81	78	75	74	74	76	74	73	72		
6	F	88	87	90	93	97	93	87	90	85	87	86	92	85	93	87	87		
7	G	97	99	98	94	72	119	107	98	87	97	98	94	92	67	86	84		
8	H	92	103	88	93	64	82	64	80	78	81	82	85	86	95	87	94		
9	I	102	101	97	92	83	126	102	95	86	86	88	83	87	85	85	83		
10	J	90	90	89	88	80	90	90	86	85	87	91	87	87	86	84	86		
11	K	104	98	86	77	73	93	94	88	87	83	82	80	79	76	75	75		
12	L	112	113	120	110	90	140	116	116	113	113	108	97	95	96	97	95		
13	M	107	108	106	81	75	103	92	86	87	85	84	83	83	82	84	83		
14	N	110	107	103	104	100	102	97	92	96	98	91	85	96	88	91	85		
15	O	87	85	91	77	77	107	105	103	100	98	97	92	87	87	88	86		
16	P	85	90	102	95	93	99	94	87	80	82	84	84	82	81	84	78		
17	Q	94	96	102	91	87	102	94	89	86	86	83	82	77	77	77	74		
18	R	81	87	94	80	99	108	96	93	89	88	87	86	83	83	83	79		
19	S	88	86	87	83	83	98	95	93	87	86	97	103	102	97	95	92		
20	T	104	105	105	92	73	103	95	94	93	92	91	88	87	83	79	83		
21	U	87	95	93	89	93	109	94	99	101	89	86	84	83	81	79	74		
22	V	80	81	75	78	71	85	83	84	82	83	83	87	88	84	83	85		
23	W	107	105	98	99	94	103	98	97	96	94	94	92	92	94	94	91		
24	X	85	87	86	85	78	87	83	87	83	80	79	82	83	84	83	81		
25	Y	90	89	91	87	77	93	92	91	89	85	85	86	82	80	80	76		
26	Z	85	83	89	87	69	103	88	90	89	69	69	73	69	70	71	66		
27	AA	86	86	82	80	68	93	72	75	68	67	68	68	66	70	69	67		
28	AB	85	83	81	79	73	85	84	82	80	79	78	78	78	77	79	76		
29	AC	90	83	87	87	85	93	90	87	85	85	86	83	82	79	79	79		
30	AD	93	87	85	88	83	94	91	87	84	86	86	86	83	76	77	78		
31	AE	88	88	86	82	76	94	88	87	86	87	87	85	83	85	85	86		
32	AF	85	82	79	82	77	92	91	90	88	87	88	86	86	85	86	85		
33	AG	99	98	96	93	85	96	84	79	73	74	78	77	78	74	74	79		
34	AH	88	87	86	90	74	92	91	86	86	86	86	80	75	79	75	74		
35	AI	89	89	87	83	79	89	88	81	84	80	80	85	85	80	78	76		
36	AJ	87	86	86	88	76	86	84	83	80	82	81	80	78	77	79	79		
37	AK	93	93	91	89	79	97	95	93	91	90	88	86	83	81	81	79		
38	AL	74	76	74	73	64	91	89	88	87	87	85	84	83	82	81	78		
39	AM	86	89	90	89	86	101	93	98	98	97	87	95	87	86	82	86		
40	AN	96	94	93	90	87	119	107	96	90	86	84	85	84	89	85	81		
41	AO	87	87	90	87	85	96	94	82	85	83	87	86	85	87	84	83		
42	AP	85	86	85	86	77	89	77	79	80	81	82	80	81	81	79	77		
43	AQ	93	95	93	92	75	93	92	90	82	80	81	84	83	81	79	80		
44	AR	89	90	97	89	77	83	83	83	88	83	84	82	83	84	83	82		
45	AS	86	86	85	80	77	88	88	85	84	80	81	79	80	80	80	79		
46	AT	85	82	81	85	78	80	79	60	80	75	71	72	73	72	81	80		
47	AU	87	91	89	91	69	98	97	97	92	92	90	87	87	88	86	83		
48	AV	79	80	81	80	76	91	90	90	89	84	83	81	80	77	80	75		
49	AW	78	76	76	75	71	93	92	90	89	89	85	83	80	83	79	77		
50	AX	91	89	87	92	77	85	82	83	81	81	82	81	79	76	77	78		
51	AY	82	81	82	82	77	88	86	83	85	82	79	77	79	78	77	75		
52	AZ	85	85	84	82	79	89	87	85	85	79	79	80	78	75	76	72		
53	BA	85	86	85	83	77	100	98	97	95	93	93	90	90	89	85	83		
54	BB	76	75	78	73	73	90	89	89	86	85	84	83	80	78	76	77		
55	BC	85	85	83	78	81	91	82	75	71	69	70	71	72	81	82	72		
56	BD	96	95	91	94	86	99	97	93	91	89	85	83	80	78	77	80		
57	BE	86	85	86	86	85	91	89	88	87	84	83	88	80	79	78	75		
58	BF	80	79	81	79	68	90	87	79	76	72	70	81	79	79	78	76		
59	BG	89	89	87	87	73	106	103	104	104	102	104	103	95	92	87	82		
60	BH	84	83	81	80	73	86	85	84	82	81	82	79	80	77	73	73		
61	BI	72	72	70	72	63	79	78	82	77	76	78	76	73	68	73	67		
62	BJ	79	78	82	80	74	89	86	84	81	78	75	79	76	73	75	72		
63	BK	80	78	79	78	72	99	98	98	95	94	93	94	91	89	86	83		

Serial No.	Study Code	Study Group	Name	Age	Sex	MRD no.	Height (cm)	height (m)	Weight(Kg)	BMI (Kg/m2)	ASA grade	Mallam pati class	Thyrome ntral distance	Comorbidities	Induction dose of propofol (mg)	Cormack lehane classification	Time of intubation(se cs)	Heart Rate_Before nebulisation	Heart Rate_During Nebulisation 5 min	Heart Rate_During Nebulisation 10 min	Heart Rate_After Nebulisation 5th min	Heart Rate_After Nebulisation 10th min	Heart Rate_Just before intubation	Heart Rate_Immediately after intubation
64	BL	2	VG	38	M	1102973	173	1.73	75	25.1	I	1	>6.5cm	No	100	1	15	80	79	78	77	78	69	82
65	BM	0	MK	25	F	1219306	160	1.6	70	27.3	I	1	>6.5cm	No	150	2a	13	68	69	68	65	67	60	118
66	BN	1	P	23	F	405725	160	1.6	50	19.5	I	1	>6.5cm	No	100	2a	14	80	80	78	75	74	68	79
67	BO	0	S	41	F	1225141	163	1.63	70	26.3	I	2	>6.5cm	No	120	2a	15	88	87	88	85	86	75	95
68	BP	0	SDD	34	M	12009972	175	1.75	85	27.8	II	2	>6.5cm	No	200	2b	14	110	110	109	108	109	77	99
69	BQ	0	S	36	F	1224875	168	1.68	80	28.3	I	2	>6.5cm	No	150	2a	13	86	87	88	86	85	65	98
70	BR	2	SM	33	F	1206269	155	1.55	65	27.1	II	2	>6.5cm	Hypothyroid	90	2a	12	83	83	82	85	88	87	90
71	BS	1	S	40	M	1226321	168	1.68	70	24.8	I	2	>6.5cm	No	150	2a	13	85	84	80	78	80	72	86
72	BT	0	BK	54	F	1227085	157	1.57	60	24.3	I	2	>6.5cm	No	100	1	14	85	86	85	84	84	80	99
73	BU	1	M	39	F	590277	163	1.63	75	28.2	I	2	>6.5cm	No	100	2a	12	78	77	76	77	78	70	85
74	BV	1	C	45	F	124165	160	1.6	65	25.4	II	2	>6.5cm	T2DM	80	2a	15	89	85	84	80	82	78	90
75	BW	2	S	35	F	1241234	155	1.55	80	33.3	I	2	>6.5cm	No	100	2a	15	85	83	80	78	78	69	78
76	BX	1	A	33	F	1241075	160	1.6	70	27.3	I	2	>6.5cm	No	100	2a	14	85	84	82	6	79	75	88
77	BY	0	M	59	F	1233818	157	1.57	60	24.3	I	2	>6.5cm	No	120	1	12	68	67	69	68	70	60	79
78	BZ	1	GK	31	F	1240728	162	1.62	80	30.5	I	2	>6.5cm	No	140	2a	16	80	80	79	77	79	69	100
79	CA	0	GS	25	M	1234932	172	1.72	80	27.0	I	2	>6.5cm	No	100	2a	14	70	70	72	70	68	60	98
80	CB	1	B	30	M	94364	157	1.57	60	24.3	II	2	>6.5cm	T2DM	80	2a	12	68	69	70	68	67	60	85
81	CC	2	PK	67	M	1240027	160	1.6	70	27.3	I	2	>6.5cm	No	100	1	13	82	81	82	80	82	75	90
82	CD	2	N	26	F	2157558	157	1.57	45	18.3	I	1	>6.5cm	No	80	1	15	75	73	70	72	73	68	76
83	CE	2	P	41	M	476460	162	1.62	70	26.7	I	2	>6.5cm	No	80	2a	14	88	85	83	80	80	70	85
84	CF	2	K	35	F	1244554	162	1.62	61	23.2	I	1	>6.5cm	No	90	1	15	69	65	64	62	62	58	72
85	CG	1	S	28	F	1245428	163	1.63	70	26.3	I	2	>6.5cm	No	100	2a	15	85	84	80	79	75	68	99
86	CH	1	V	32	M	1247393	170	1.7	80	27.7	I	2	>6.5cm	No	120	2a	15	75	73	74	70	69	63	79
87	CI	0	C	25	M	1245611	155	1.55	45	18.7	I	2	>6.5cm	No	100	1	14	99	98	95	97	96	90	112
88	CJ	1	M	30	F	842794	163	1.63	60	22.6	I	2	>6.5cm	No	100	1	14	82	81	82	85	84	65	85
89	CK	1	D	35	M	1247990	178	1.78	100	31.6	II	2	>6.5cm	Overweight	150	2b	15	81	80	75	74	76	65	79
90	CL	0	G	33	M	1247599	165	1.65	75	27.5	II	2	>6.5cm	HTN	120	2a	14	65	66	68	66	69	59	80
91	CM	2	S	19	F	718287	167	1.67	60	21.5	I	1	>6.5cm	No	80	1	15	80	78	75	74	76	68	75
92	CN	1	A	24	F	1248160	178	1.78	65	20.5	II	2	>6.5cm	CHRONIC ALCOHOLIC	100	2a	16	84	83	80	78	80	75	90
93	CO	1	R	23	F	674827	160	1.6	60	23.4	I	2	>6.5cm	No	80	1	15	85	85	84	85	85	82	98
94	CP	0	MD	55	F	1251883	165	1.65	70	25.7	I	2	>6.5cm	No	140	2a	13	68	69	68	70	69	60	98
95	CQ	0	A	31	M	1016860	162	1.62	70	26.7	II	1	>6.5cm	CHRONIC SMOKER	130	1	14	84	85	84	83	85	74	90
96	CR	2	N	36	F	1246364	160	1.6	70	27.3	I	1	>6.5cm	No	80	1	14	79	77	75	73	73	68	78
97	CS	1	L	34	M	1232064	167	1.67	70	25.1	I	2	>6.5cm	No	100	2a	16	84	84	83	80	79	68	99
98	CT	0	D	22	M	1254549	165	1.65	55	20.2	I	2	>6.5cm	No	110	2a	15	79	78	80	79		70	98
99	CU	0	i	61	F	1257805	162	1.62	68	25.9	I	2	>6.5cm	No	120	2b	14	94	93	94	95	94	85	112
100	CV	2	K	42	F	1261555	152	1.52	65	28.1	II	2	>6.5cm	Hypothyroid	80	2a	14	68	65	63	60	60	54	80
101	CW	0	R	40	F	1249903	160	1.6	65	25.4	I	2	>6.5cm	No	110	2a	15	69	69	70	68	68	60	78
102	CX	1	J	27	M	1237308	165	1.65	80	29.4	I	2	>6.5cm	No	120	2a	16	83	82	80	79	80	75	95
103	CY	2	V	62	F	1262808	162	1.62	70	26.7	I	1	>6.5cm	No	80	1	14	59	58	58	57	58	55	63
104	CZ	1	S	32	F	1262074	157	1.57	65	26.4	I	2	>6.5cm	No	110	2a	15	83	80	82	80	79	70	90
105	DA	0	R	49	F	1262371	162	1.62	70	26.7	I	1	>6.5cm	No	120	1	15	80	79	80	81	80	70	92
106	DB	2	C	76	F	1253748	162	1.62	65	24.8	II	2	>6.5cm	T2DM	80	1	14	105	104	100	99	100	90	108
107	DC	0	SD	19	F	1264402	152	1.52	40	17.3	I	1	>6.5cm	No	80	1	14	69	68	69	68	69	65	80
108	DD	0	H	37	M	1240707	178	1.78	52	16.4	I	1	>6.5cm	No	100	1	12	99	99	98	97	99	86	110
109	DE	0	P	34	F	1265579	160	1.6	65	25.4	I	2	>6.5cm	No	120	2a	14	85	84	85	85	84	70	
110	DF	1	R	23	M	1262479	172	1.72	65	22.0	I	1	>6.5cm	No	120	2a	15	84	84	83	80	81	75	88
111	DG	1	S	31	M	1267820	188	1.88	95	26.9	II	2	>6.5cm	HTN	120	2a	16	73	72	70	69	69	64	80
112	DH	2	N	35	F	1160361	147	1.47	60	27.8	I	2	>6.5cm	No	80	2a	15	75	70	70	68	65	60	73
113	DI	2	J	53	M	1277168	165	1.65	84	30.9	I	2	>6.5cm	No	120	2a	16	68	64	65	63	62	58	70
114	DJ	0	R	32	F	1280609	163	1.63	70	26.3	I	2	>6.5cm	No	120	2a	16	80	78	79	80	85	78	95
115	DK	2	H	79	M	1296688	177	1.77	70	22.3	I	2	>6.5cm	No	110	2a	15	70	70	71	72	72	65	84
116	DL	1	A	50	F	1235496	155	1.55	45	18.7	I	1	>6.5cm	No	80	1	18	62	61	63	65	64	60	84
117	DM	2	B	51	F	1296719	157	1.57	65	26.4	II	2	>6.5cm	HTN	70	1	15	98	98	97	98	98	90	115
118	DN	0	U	55	M	1355712	175	1.75	85	27.8	I	1	>6.5cm	No	150	2b	15	75	75	74	76	75	70	98
119	DO	0	GS	60	M	1296165	178	1.78	70	22.1	I	2	>6.5cm	No	100	2a	16	85	84	84	82	84	78	114
120	DP	1	A	23	M	1285767	178	1.78	70	22.1	I	2	>6.5cm	No	120	2a	16	74	70	70	72	68	65	75
121	DQ	1	N	45	F	1321901	162	1.62	70	26.7	I	2	>6.5cm	No	120	2a	14	100	98	99	99	98	88	115
122	DR	1	KR	30	F	1321767	165	1.65	75	27.5	I	1	>6.5cm	No	120	2a	14	68	68	67	69	68	65	74
123	DS	0	S	49	F	1321812	157	1.57	55	22.3	I	1	>6.5cm	No	100	1	17	95	96	97	95	96	90	115
124	DT	2	VLS	45	F	1251389	170	1.7	65	22.5	I	2	>6.5cm	No	100	2a	14	84	83	85	82	84	80	99
125	DU	2	G	43	M	1317844	173	1.73	120	40.1	I	2	>6.5cm	No	150	2a	17	75	75	74	76	76	70	80
126	DV	2	G	32	M	1256389	152	1.52	60	26.0	I	1	>6.5cm	No	100	1	13	84	82	79	80	80	69	85

Serial No.	Study Code	Heart Rate_1 min	Heart Rate_2 min	Heart Rate_3 min	Heart Rate_4 min	Heart Rate_5 min	Heart Rate_6 min	Heart Rate_7 min	Heart Rate_8 min	Heart Rate_9 min	Heart Rate_10 min	SpO2_Before nebulisation	SpO2_During Nebulisation 5 min	SpO2_During Nebulisation 10 min	SpO2_After Nebulisation 5th min	SpO2_After Nebulisation 10th min	SpO2_Just before intubation	SpO2_Immediately after intubation	SpO2_1 min	SpO2_2 min	SpO2_3 min
64	BL	80	78	77	75	74	72	70	72	68	65	100	100	100	99	100	100	100	99	100	100
65	BM	116	117	118	115	110	112	114	110	98	96	99	99	100	99	100	100	100	100	100	100
66	BN	78	77	75	74	70	68	66	67	69	68	99	99	100	100	99	100	100	99	100	100
67	BO	95	96	94	95	95	92	90	88	89	86	99	99	100	99	99	100	100	99	100	100
68	BP	98	98	95	95	95	94	95	93	84	84	99	99	99	99	99	99	99	99	99	99
69	BQ	97	90	92	90	88	85	87	85	83	80	99	98	99	98	98	98	99	99	99	99
70	BR	83	84	83	82	82	82	81	80	80	77	99	99	99	99	99	98	99	99	99	99
71	BS	84	83	82	80	79	78	75	73	70	71	98	99	98	99	98	99	99	100	100	100
72	BT	100	103	100	102	100	98	96	94	93	90	98	97	98	99	98	99	100	99	100	100
73	BU	84	85	82	80	79	77	77	76	75	75	100	100	100	99	100	100	100	100	100	100
74	BV	89	85	80	78	75	76	79	80	78	75	100	100	100	99	100	100	100	100	100	100
75	BW	75	73	70	68	65	66	68	69	65	63	99	100	99	100	100	100	100	100	100	99
76	BX	86	84	80	78	80	82	81	79	77	76	100	100	99	100	100	100	100	100	100	100
77	BY	78	77	75	75	74	73	74	72	71	70	100	100	100	100	100	100	100	100	100	100
78	BZ	99	95	94	96	94	94	96	97	95	94	100	100	100	100	100	100	100	100	100	100
79	CA	98	97	95	94	96	93	92	90	90	88	100	100	100	100	100	100	100	100	100	100
80	CB	84	82	80	78	80	79	78	77	78	75	98	98	97	99	99	100	99	99	99	99
81	CC	88	87	86	85	83	82	80	82	78	77	100	100	100	100	100	100	100	100	100	100
82	CD	74	70	72	71	69	65	64	63	62	60	99	100	100	100	100	100	100	100	100	100
83	CE	84	80	78	75	79	78	75	74	73	72	100	100	100	100	100	100	100	100	100	100
84	CF	70	69	65	64	63	66	64	63	60	58	99	100	99	100	100	100	100	99	100	99
85	CG	95	94	96	93	90	88	89	87	85	82	100	100	100	100	100	100	100	100	100	100
86	CH	75	70	72	69	65	64	62	60	61	60	98	97	98	98	98	98	99	99	99	98
87	CI	110	113	112	110	108	105	107	109	105	100	100	100	100	98	100	100	100	100	100	100
88	CJ	82	80	78	80	75	74	72	70	68	65	99	99	100	100	100	99	100	100	100	99
89	CK	75	74	76	74	75	73	70	71	69	68	98	99	99	99	98	99	99	99	99	99
90	CL	78	75	70	68	69	71	68	65	63	63	99	100	99	100	99	100	100	100	100	100
91	CM	73	70	71	70	69	70	68	67	65	66	100	100	100	100	100	100	100	100	100	100
92	CN	88	91	87	85	84	83	84	80	80	78	100	100	100	100	100	100	100	100	100	100
93	CO	97	97	96	94	94	95	97	94	92	92	99	99	99	99	99	99	99	99	99	99
94	CP	87	85	84	83	80	78	79	75	70	68	96	97	96	99	96	98	98	99	97	98
95	CQ	88	85	87	88	85	84	84	83	83	83	100	100	100	100	100	100	100	99	99	99
96	CR	77	75	73	72	70	71	70	69	70	70	99	100	100	100	100	100	100	100	100	99
97	CS	97	95	94	90	89	90	88	85	87	83	98	98	97	98	98	99	99	99	99	99
98	CT	97	95	94	93	90	88	85	82	80	78	99	100	100	99	100	100	100	99	99	100
99	CU	110	111	108	103	100	102	98	95	96	93	100	100	100	100	100	100	100	99	100	100
100	CV	78	76	74	73	75	70	69	68	67	66	99	100	100	100	100	100	100	100	100	100
101	CW	78	75	74	73	70	70	70	69	69	69	99	99	99	99	99	100	100	100	100	100
102	CX	93	94	93	93	92	91	90	91	89	85	99	98	98	98	97	98	99	99	99	99
103	CY	63	62	60	59	58	58	57	59	60	58	100	100	100	100	100	100	100	100	100	100
104	CZ	89	88	85	83	82	82	81	80	79	79	100	100	100	100	100	100	100	100	100	100
105	DA	90	88	87	85	84	83	84	82	80	78	100	100	100	100	100	100	100	100	100	100
106	DB	105	100	99	98	95	94	93	94	93	92	99	99	99	99	100	100	100	100	100	99
107	DC	78	77	79	78	76	74	70	68	65	64	100	100	100	100	100	100	100	100	100	100
108	DD	109	102	108	105	102	100	99	98	98	99	100	100	100	100	100	100	100	100	100	100
109	DE	98	95	94	92	88	85	84	83	80	79	99	98	99	99	99	100	100	100	100	99
110	DF	86	85	84	82	80	79	78	75	74	72	99	99	98	99	100	100	100	99	99	100
111	DG	79	78	79	77	75	74	72	73	76	74	99	100	100	100	100	100	100	100	100	100
112	DH	70	69	69	69	68	65	65	65	66	64	100	100	100	100	100	100	100	100	100	100
113	DI	69	65	64	66	68	65	66	65	64	63	99	99	99	100	99	100	100	100	100	100
114	DJ	94	95	96	94	93	90	92	90	88	86	100	100	100	99	100	100	100	100	100	100
115	DK	82	80	78	78	74	75	74	72	73	72	100	100	100	100	100	100	100	100	100	100
116	DL	82	80	78	79	77	76	78	75	74	72	100	100	100	100	100	100	100	100	100	100
117	DM	114	112	110	108	106	105	104	100	99	98	100	100	100	100	100	100	100	100	100	100
118	DN	97	95	90	88	87	85	82	83	80	80	100	100	100	100	100	100	100	100	100	100
119	DO	112	100	100	98	95	93	92	92	90	88	99	99	99	100	100	100	100	99	99	99
120	DP	73	72	70	68	65	66	65	65	64	64	100	100	100	100	100	100	100	100	100	100
121	DQ	114	110	108	106	108	105	104	100	98	96	99	98	99	98	98	98	99	99	98	99
122	DR	73	74	70	70	75	72	70	68	65	63	100	100	100	100	100	100	100	100	100	100
123	DS	113	110	108	107	105	104	105	100	98	96	100	100	100	100	100	100	100	100	100	100
124	DT	99	98	95	92	90	90	88	86	85	86	100	100	100	100	100	100	100	100	98	99
125	DU	78	77	78	76	74	73	72	70	70	70	99	99	99	99	99	99	100	100	100	100
126	DV	83	80	79	79	80	75	73	75	74	74	100	100	100	100	100	100	100	100	100	100

Serial No.	Study Code	SpO2_4 min	SpO2_5 min	SpO2_6 min	SpO2_7 min	SpO2_8 min	SpO2_9 min	SpO2_10 min	SBP_Before nebulisation	SBP_During Nebulisation 5 min	SBP_During Nebulisation 10 min	SBP_After Nebulisation 5th min	SBP_After Nebulisation 10th min	SBP_Just before intubation	SBP_Immediately after intubation	SBP_1 min	SBP_2 min	SBP_3 min	SBP_4 min	SBP_5 min	SBP_6 min	SBP_7 min	SBP_8 min	SBP_9 min	SBP_10 min
64	BL	100	100	100	100	100	100	100	118	118	116	117	118	105	118	116	115	110	110	109	110	109	106	107	102
65	BM	100	100	100	100	100	100	100	120	120	118	120	116	98	140	138	140	136	135	134	130	128	128	125	120
66	BN	100	100	100	100	100	100	100	126	126	125	124	120	110	129	128	126	127	125	124	122	118	116	108	102
67	BO	99	100	100	100	100	100	100	110	112	110	112	110	100	129	130	129	125	124	124	126	122	120	118	116
68	BP	99	99	99	99	99	99	99	140	138	140	139	140	119	151	148	148	135	134	130	128	128	127	127	125
69	BQ	99	97	98	98	98	98	98	126	126	128	125	126	100	139	135	132	133	129	125	120	122	118	116	112
70	BR	99	99	99	98	99	99	98	130	130	128	119	115	104	130	133	129	119	112	115	106	106	103	103	100
71	BS	100	100	100	100	100	100	100	120	118	120	118	116	100	125	124	122	120	118	116	115	112	110	108	112
72	BT	100	99	98	99	100	100	100	134	134	132	130	131	120	140	138	138	135	136	132	130	130	129	128	129
73	BU	100	100	100	100	100	100	100	120	122	120	120	118	110	126	126	125	124	122	120	118	117	118	116	115
74	BV	100	100	99	100	99	100	100	120	118	116	118	115	110	122	120	119	119	118	115	114	113	108	106	100
75	BW	100	99	100	100	100	100	100	118	118	116	115	116	110	121	120	118	119	120	118	116	109	105	108	101
76	BX	100	99	100	100	100	100	100	130	128	127	126	125	118	129	127	126	125	123	120	118	116	115	113	112
77	BY	100	100	100	100	100	100	100	110	111	110	111	112	98	130	130	129	128	125	124	122	120	118	116	116
78	BZ	100	100	100	100	100	100	100	120	118	118	116	115	102	130	130	128	128	130	125	124	122	120	118	115
79	CA	100	100	100	100	100	100	100	128	125	124	126	120	110	140	138	135	134	132	130	131	125	124	122	120
80	CB	99	99	99	99	99	99	99	126	125	124	122	124	110	128	128	126	124	122	120	120	118	116	118	116
81	CC	100	100	100	100	100	100	100	116	117	118	120	116	100	115	114	113	112	110	112	111	110	114	112	108
82	CD	100	100	100	100	100	100	100	116	110	112	111	112	104	120	116	114	113	110	118	112	110	109	108	104
83	CE	100	100	100	100	100	100	100	116	116	110	108	111	100	115	116	110	108	105	103	100	102	98	100	95
84	CF	100	100	100	100	100	100	100	120	120	118	116	112	104	120	118	116	118	115	114	113	112	110	114	110
85	CG	100	100	100	100	100	100	100	116	115	118	120	117	110	125	120	118	116	110	112	110	108	102	100	99
86	CH	98	98	98	98	98	98	98	118	116	115	114	113	102	125	124	120	118	116	115	110	113	112	110	109
87	CI	100	100	100	100	100	100	100	120	122	120	120	119	108	139	135	134	133	130	129	128	120	118	115	110
88	CJ	99	100	100	100	100	100	100	115	114	112	113	114	104	124	123	122	120	118	115	114	112	111	110	110
89	CK	98	99	99	99	99	99	99	116	115	113	110	110	100	129	129	128	127	125	123	120	121	120	118	113
90	CL	100	100	100	100	100	100	100	108	110	105	108	106	95	139	138	135	130	130	131	129	125	118	110	108
91	CM	100	100	100	100	100	100	100	111	112	110	110	111	100	118	114	110	112	110	108	105	100	98	98	98
92	CN	100	100	100	100	100	100	100	112	110	111	109	110	99	120	118	120	115	110	112	110	109	105	102	99
93	CO	99	99	99	99	99	99	99	126	128	125	127	125	110	139	131	134	123	126	112	120	118	125	118	120
94	CP	97	97	98	98	98	98	97	129	130	128	125	128	100	140	138	140	135	134	133	130	129	125	120	118
95	CQ	100	99	99	99	99	99	99	117	118	120	118	116	100	129	129	125	124	120	120	118	116	114	110	108
96	CR	100	100	100	100	100	100	100	123	120	118	120	118	110	120	119	120	116	113	110	111	108	106	105	100
97	CS	99	98	97	98	98	98	99	118	118	115	110	112	99	129	125	123	120	118	116	110	109	110	107	105
98	CT	100	100	100	100	100	100	100	132	130	130	130	129	100	158	140	125	123	125	118	117	115	110	118	120
99	CU	100	100	100	100	100	100	100	129	130	128	130	128	115	140	140	138	135	136	132	130	128	124	120	118
100	CV	100	100	100	100	100	100	100	116	115	113	110	108	98	118	116	114	110	108	105	102	100	101	102	99
101	CW	99	100	99	100	99	99	99	129	128	130	130	128	115	138	135	134	133	130	128	125	124	120	118	115
102	CX	99	98	99	99	99	98	99	118	117	116	116	115	104	129	128	125	120	118	116	115	110	109	108	110
103	CY	100	100	100	100	100	100	100	117	118	109	105	103	98	120	118	116	115	110	109	108	105	104	107	103
104	CZ	100	100	100	100	100	100	100	120	119	120	118	115	101	125	124	123	120	118	117	108	107	105	104	100
105	DA	100	100	100	100	100	100	100	129	128	128	130	129	110	140	138	135	135	130	129	127	125	120	121	120
106	DB	100	99	100	100	100	99	99	136	135	130	128	128	120	130	128	128	130	128	125	120	122	121	125	124
107	DC	100	100	100	100	100	100	100	100	100	98	99	100	95	128	125	124	122	118	116	116	112	108	105	101
108	DD	100	100	100	100	100	100	100	120	121	120	118	120	110	133	132	130	129	128	125	122	120	118	116	112
109	DE	100	100	100	99	100	100	100	132	130	132	130	129	100	135	138	135	134	132	130	129	128	127	125	124
110	DF	100	99	100	99	100	100	100	118	116	115	115	115	105	124	122	124	125	124	122	120	118	115	114	110
111	DG	100	100	100	100	100	100	100	120	118	118	118	116	110	128	126	124	122	120	118	116	115	114	112	110
112	DH	100	100	100	100	100	100	100	116	116	115	114	110	98	119	115	114	112	110	108	105	104	102	102	100
113	DI	100	100	100	100	100	100	100	138	138	140	135	130	118	139	138	130	128	130	129	128	125	124	124	120
114	DJ	99	100	99	100	100	99	100	128	125	124	125	126	108	140	138	130	128	125	124	122	120	120	118	120
115	DK	100	100	100	100	100	100	100	116	115	118	116	115	110	122	121	120	118	118	116	115	114	112	112	108
116	DL	100	100	100	100	100	100	100	120	120	119	120	118	105	122	121	120	118	116	117	116	115	114	113	110
117	DM	100	100	100	100	100	100	100	138	140	142	138	140	130	150	150	148	148	145	140	138	130	128	127	118
118	DN	100	100	100	100	100	100	100	112	112	114	114	112	90	130	128	128	126	125	124	120	118	117	116	115
119	DO	99	100	99	99	100	99	99	118	116	115	120	117	100	138	136	138	132	128	125	124	125	123	122	120
120	DP	100	100	100	100	100	100	100	120	118	118	120	118	100	128	128	130	125	118	105	100	98	97	98	95
121	DQ	98	99	98	98	98	98	98	150	148	145	145	145	120	155	150	148	148	145	142	140	142	140	138	135
122	DR	100	100	100	100	100	100	100	140	140	138	138	135	118	135	134	132	130	128	125	124	124	122	124	125
123	DS	100	100	100	100	100	100	100	135	135	134	135	130	118	140	138	135	130	130	128	125	127	125	125	124
124	DT	100	99	100	100	100	100	100	108	112	111	110	115	85	118	115	116	115	114	113	115	112	111	112	100
125	DU	100	100	100	100	100	100	100	108	112	110	108	90	118	116	114	112	114	110	110	111	112	110	112	105
126	DV	100	100	100	100	100	99	100	114	114	115	114	115	100	120	118	115	110	105	100	100	98	95	100	100

Serial No.	Study Code	DBP_Before nebulisation	DBP_During Nebulisation 5 min	DBP_During Nebulisation 10 min	DBP_After Nebulisation 5th min	DBP_After Nebulisation 10th min	DBP_Just before intubation	DBP_Immediately after intubation	DBP_1 min	DBP_2 min	DBP_3 min	DBP_4 min	DBP_5 min	DBP_6 min	DBP_7 min	DBP_8 min	DBP_9 min	DBP_10 min	MAP_Before nebulisation
64	BL	85	83	80	84	82	60	68	65	64	60	62	60	59	60	59	58	55	96
65	BM	68	65	66	65	67	60	80	79	82	78	76	78	74	72	70	70	62	85
66	BN	84	80	82	80	80	66	82	80	78	77	73	70	68	65	58	61	60	98
67	BO	65	65	66	64	66	60	72	70	70	68	65	62	60	62	60	58	58	80
68	BP	90	88	92	90	91	73	105	114	92	90	90	88	88	86	80	80	80	107
69	BQ	80	79	75	76	74	60	82	80	78	80	78	75	80	80	70	69	70	95
70	BR	85	82	84	80	75	63	95	81	86	85	71	67	64	55	58	55	56	100
71	BS	76	75	74	78	75	61	78	77	73	72	71	72	70	68	67	65	60	91
72	BT	70	69	70	71	69	65	72	70	72	70	74	73	72	71	70	72	70	91
73	BU	65	64	62	65	65	60	70	68	70	68	66	70	68	68	62	60	60	83
74	BV	70	68	65	64	64	60	69	68	66	68	67	65	70	69	58	61	60	87
75	BW	70	67	72	70	71	68	74	73	70	69	65	60	59	61	63	60	64	86
76	BX	69	65	65	64	65	60	71	70	68	67	66	65	64	60	60	60	59	89
77	BY	65	65	64	65	64	60	78	75	74	75	74	72	70	70	68	65	66	80
78	BZ	70	68	70	70	69	58	76	73	72	70	68	70	68	65	60	60	60	87
79	CA	70	72	70	72	70	68	79	78	74	72	70	68	71	70	68	65	60	89
80	CB	72	74	72	70	68	60	68	68	66	63	62	62	60	60	56	54	58	90
81	CC	65	65	65	64	64	60	68	66	67	65	64	60	58	56	5	54	54	82
82	CD	81	77	78	80	75	68	80	68	70	69	59	54	60	59	59	58	55	93
83	CE	65	62	60	62	59	55	68	65	60	59	60	58	60	58	55	54	55	82
84	CF	81	79	80	78	80	70	80	79	75	73	70	69	70	68	70	68	65	94
85	CG	50	49	52	50	50	48	63	60	58	58	60	64	59	61	58	59	58	72
86	CH	70	69	68	65	66	60	70	66	68	67	66	65	70	68	63	60	59	86
87	CI	65	64	66	65	64	60	72	70	68	69	65	64	65	60	59	60	60	83
88	CJ	66	68	65	66	67	60	74	73	72	70	71	70	68	65	62	63	60	82
89	CK	80	80	79	75	78	60	77	76	77	76	78	79	75	73	72	79	79	92
90	CL	60	60	62	60	61	58	75	74	70	68	72	70	69	65	68	60	60	76
91	CM	65	62	60	62	61	59	64	60	62	60	61	60	58	59	60	58	55	80
92	CN	60	60	63	60	58	50	67	68	66	63	58	58	58	60	58	58	60	77
93	CO	72	70	72	70	70	70	82	86	79	79	69	73	71	72	63	70	68	90
94	CP	69	69	67	70	65	55	79	78	75	75	74	70	69	69	65	64	60	89
95	CQ	80	80	79	79	78	55	89	88	87	85	83	82	81	80	80	68	65	92
96	CR	66	65	65	65	64	60	68	68	65	64	62	65	63	61	62	60	60	85
97	CS	70	69	70	69	65	63	78	78	77	73	72	70	70	69	66	65	69	86
98	CT	69	69	70	68	70	60	88	80	78	70	68	65	63	64	68	70	65	90
99	CU	85	84	85	84	83	68	99	98	95	94	90	90	89	85	83	80	79	100
100	CV	67	66	70	68	65	60	72	70	69	65	63	60	59	59	58	60	60	83
101	CW	68	67	68	65	66	60	72	70	69	68	70	68	65	63	60	60	58	88
102	CX	75	73	74	73	73	68	78	78	73	68	66	65	65	64	61	60	58	89
103	CY	72	67	68	65	62	58	70	68	65	63	62	62	63	65	66	65	62	87
104	CZ	70	70	69	70	65	60	73	68	66	63	62	60	60	59	53	52	54	87
105	DA	76	75	76	75	74	62	79	78	75	74	73	72	71	72	70	70	69	94
106	DB	71	70	70	71	70	68	70	68	65	60	63	64	64	65	60	61	59	93
107	DC	60	59	58	60	56	55	75	74	72	70	68	65	60	62	60	60	59	73
108	DD	60	60	62	59	58	50	63	60	60	61	60	59	58	56	57	58	60	80
109	DE	71	70	70	69	70	62	70	69	68	65	62	60	61	60	60	59	60	91
110	DF	75	76	74	75	74	69	76	74	72	73	72	72	70	68	68	69	70	89
111	DG	72	70	71	69	65	60	72	68	70	68	67	65	64	66	63	60	62	88
112	DH	67	67	69	71	68	60	71	70	70	70	69	65	66	65	66	65	60	83
113	DI	66	67	68	65	61	58	70	69	60	65	65	62	63	67	65	63	60	90
114	DJ	65	66	60	62	60	60	90	90	88	85	85	80	82	84	80	78	75	86
115	DK	67	65	72	70	70	60	68	68	67	65	65	70	64	62	62	60	60	83
116	DL	68	69	70	65	65	60	70	68	66	66	65	65	64	62	58	58	58	85
117	DM	69	67	72	70	74	68	74	72	74	72	70	68	65	66	60	60	59	92
118	DN	66	65	68	65	64	55	75	74	72	72	70	70	68	65	64	65	62	81
119	DO	74	70	72	68	72	60	79	78	75	70	70	68	68	70	68	68	65	89
120	DP	68	65	66	60	60	55	70	68	68	66	63	59	54	55	55	54	55	85
121	DQ	90	90	90	85	90	75	83	80	78	76	76	75	74	72	68	70	68	110
122	DR	72	70	68	70	70	60	72	72	68	66	66	65	65	64	58	62	60	95
123	DS	73	72	70	70	74	65	80	78	75	73	70	72	70	70	68	65	65	94
124	DT	72	69	74	72	68	50	80	78	75	76	78	77	75	74	72	72	65	84
125	DU	65	62	65	62	65	54	62	60	60	62	60	62	60	58	60	60	58	79
126	DV	67	65	70	70	69	60	71	70	69	68	65	63	60	59	55	50	60	83

Serial No.	Study Code	MAP_During Nebulisation 5 min	MAP_During Nebulisation 10 min	MAP_After Nebulisation 5th min	MAP_After Nebulisation 10th min	MAP_Just before intubation	MAP_Immediately after intubation	MAP_1 min	MAP_2 min	MAP_3 min	MAP_4 min	MAP_5 min	MAP_6 min	MAP_7 min	MAP_8 min	MAP_9 min	MAP_10 min	Adverse event	Treatment given
64	BL	95	92	95	94	75	85	82	81	77	78	76	76	76	75	74	71		
65	BM	83	83	83	83	73	100	99	101	97	96	97	93	91	89	88	81		
66	BN	95	96	95	93	81	98	96	94	94	90	88	86	83	77	77	74		
67	BO	81	81	80	81	73	91	90	90	87	85	83	82	82	80	78	77		
68	BP	105	108	106	107	88	120	125	111	105	105	102	101	100	96	96	95		
69	BQ	95	93	92	91	73	101	98	96	98	95	92	93	94	86	85	84		
70	BR	98	99	93	88	77	107	98	100	96	85	83	78	72	73	71	71		
71	BS	89	89	91	89	74	94	93	89	88	87	87	85	83	81	79	77		
72	BT	91	91	91	90	83	95	93	94	92	95	93	91	91	90	91	90		
73	BU	83	81	83	83	77	89	87	88	87	85	87	85	84	81	79	78		
74	BV	85	82	82	81	77	87	85	84	85	84	82	85	84	75	76	73		
75	BW	84	87	85	86	82	90	89	86	86	83	79	78	77	77	76	76		
76	BX	86	86	85	85	79	90	89	87	86	85	83	82	79	78	78	77		
77	BY	80	79	80	80	73	95	93	92	93	91	89	87	87	85	82	83		
78	BZ	85	86	85	84	73	94	92	91	89	89	88	87	84	80	79	78		
79	CA	90	88	90	87	82	99	98	94	93	91	89	91	88	87	84	80		
80	CB	91	89	87	87	77	88	88	86	83	82	81	80	79	76	75	77		
81	CC	82	83	83	81	73	84	82	82	81	79	77	76	74	41	73	72		
82	CD	88	89	90	87	80	93	84	85	84	76	75	77	76	76	75	71		
83	CE	80	77	77	76	70	84	82	77	75	75	73	73	73	69	69	68		
84	CF	93	93	91	91	81	93	92	89	88	85	84	84	83	83	83	80		
85	CG	71	74	73	72	69	84	80	78	77	77	80	76	77	73	73	72		
86	CH	85	84	81	82	74	88	85	85	84	83	82	83	83	79	77	76		
87	CI	83	84	83	82	76	94	92	90	90	87	86	86	80	79	78	77		
88	CJ	83	81	82	83	75	91	90	89	87	87	85	83	81	78	79	77		
89	CK	92	90	87	89	73	94	94	94	93	94	94	90	89	88	92	90		
90	CL	77	76	76	76	70	96	95	92	89	91	90	89	85	85	77	76		
91	CM	79	77	78	78	73	82	78	78	77	77	76	74	73	73	71	69		
92	CN	77	79	76	75	66	85	85	84	80	75	76	75	76	74	73	73		
93	CO	89	90	89	88	83	101	101	97	94	88	86	87	87	84	86	85		
94	CP	89	87	88	86	70	99	98	97	95	94	91	89	89	85	83	79		
95	CQ	93	93	92	91	70	102	102	100	98	95	95	93	92	91	82	79		
96	CR	83	83	83	82	77	85	85	83	81	79	80	79	77	77	75	73		
97	CS	85	85	83	81	75	95	94	92	89	87	85	83	82	81	79	81		
98	CT	89	90	89	90	73	111	100	94	88	87	83	81	81	82	86	83		
99	CU	99	99	99	98	84	113	112	109	108	105	104	103	99	97	93	92		
100	CV	82	84	82	79	73	87	85	84	80	78	75	73	73	72	74	73		
101	CW	87	89	87	87	78	94	92	91	90	90	88	85	83	80	79	77		
102	CX	88	88	87	87	80	95	95	90	85	83	82	82	79	77	76	75		
103	CY	84	82	78	76	71	87	85	82	80	78	78	78	78	79	79	76		
104	CZ	86	86	86	82	74	90	87	85	82	81	79	76	75	70	69	69		
105	DA	93	93	93	92	78	99	98	95	94	92	91	90	90	87	87	86		
106	DB	92	90	90	89	85	90	88	86	83	85	84	83	84	80	82	81		
107	DC	73	71	73	71	68	93	91	89	87	85	82	79	79	76	75	73		
108	DD	80	81	79	79	70	86	84	83	84	83	81	79	77	77	77	77		
109	DE	90	91	89	90	75	92	92	90	88	85	83	84	83	82	81	81		
110	DF	89	88	88	88	81	92	90	89	90	89	89	87	85	84	84	83		
111	DG	86	87	85	82	77	91	87	88	86	85	83	81	82	80	77	78		
112	DH	83	84	85	82	73	87	85	85	84	83	79	79	78	78	77	73		
113	DI	91	92	88	84	78	93	92	83	86	87	84	85	86	85	83	80		
114	DJ	86	81	83	82	76	107	106	102	99	98	95	95	96	93	91	90		
115	DK	82	87	85	85	77	86	86	85	83	83	85	81	79	79	77	76		
116	DL	86	86	83	83	75	87	86	84	83	82	82	81	80	77	76	75		
117	DM	91	95	93	96	89	99	98	99	97	95	92	89	87	83	82	79		
118	DN	81	83	81	80	67	93	92	91	90	88	88	85	83	82	82	80		
119	DO	85	86	85	87	73	99	97	96	91	89	87	87	88	86	86	83		
120	DP	83	83	80	79	70	89	88	89	86	81	74	69	69	69	69	68		
121	DQ	109	108	105	108	90	107	103	101	100	99	97	96	95	92	93	90		
122	DR	93	91	93	92	79	93	93	89	87	87	85	85	84	79	83	82		
123	DS	93	91	92	93	83	100	98	95	92	90	91	88	89	87	85	85		
124	DT	83	86	85	84	62	93	90	89	89	90	89	88	87	85	85	77		
125	DU	79	80	77	73	75	80	78	77	79	77	78	77	76	77	77	74		
126	DV	81	85	85	84	73	87	86	84	82	78	75	73	72	68	67	73		

Serial No.	Study Code	Study Group	Name	Age	Sex	MRD no.	Height (cm)	height (m)	Weight(Kg)	BMI (Kg/m2)	ASA grade	Mallam pati class	Thyrome ntral distance	Comorbidities	Induction dose of propofol (mg)	Cormack lehane classification	Time of intubation(se cs)	Heart Rate_Before nebulisation	Heart Rate_During Nebulisation 5 min	Heart Rate_During Nebulisation 10 min	Heart Rate_After Nebulisation 5th min	Heart Rate_After Nebulisation 10th min	Heart Rate_Just before intubation	Heart Rate_Immediately after intubation
127	DW	1	MM	65	F	1311904	160	1.6	55	21.5	I	1	>6.5cm	No	90	1	12	60	59	60	58	60	54	78
128	DX	2	A	45	F	1325894	160	1.6	75	29.3	I	2	>6.5cm	No	100	1	15	80	80	79	75	76	65	78
129	DY	0	U	56	F	1333019	157	1.57	70	28.4	II	1	>6.5cm	T2DM	150	1	15	75	74	74	72	72	68	98
130	DZ	2	S	51	F	1331754	175	1.75	85	27.8	II	2	>6.5cm	Hypothyroid	170	2a	16	65	64	66	68	64	62	72
131	EA	0	J	41	F	1103797	157	1.57	70	28.4	I	1	>6.5cm	No	140	2a	15	85	86	85	84	85	80	99
132	EB	0	P	71	M	1332939	155	1.55	70	29.1	I	2	>6.5cm	No	120	2a	16	65	64	66	65	64	60	80
133	EC	2	A	54	M	828950	162	1.62	80	30.5	II	2	>6.5cm	T2DM	100	2a	15	58	59	58	55	56	50	74
134	ED	1	R	48	F	411982	160	1.6	85	33.2	II	2	>6.5cm	Anaemia	150	2a	15	90	92	90	88	86	74	92
135	EE	0	S	44	F	1333430	152	1.52	65	28.1	II	1	>6.5cm	Anaemia	100	2a	18	84	82	83	84	90	75	88
136	EF	2	A	20	F	1332582	155	1.55	55	22.9	I	2	>6.5cm	No	100	2a	14	86	84	85	84	83	75	84
137	EG	2	M	38	F	1354196	165	1.65	80	29.4	I	2	>6.5cm	No	100	2a	15	95	90	88	85	84	78	94
138	EH	2	GK	46	F	1299023	152	1.52	60	26.0	I	2	>6.5cm	No	100	2b	18	94	93	90	88	85	75	90
139	EI	0	A	41	M	1283135	167	1.67	70	25.1	I	2	>6.5cm	No	120	2a	14	84	84	86	85	83	79	99
140	EJ	0	S	57	M	1307300	162	1.62	60	22.9	I	2	>6.5cm	No	120	1	13	84	85	84	88	87	80	99
141	EK	0	P	40	F	1298679	160	1.6	60	23.4	II	1	>6.5cm	HTN	120	2a	14	95	94	95	94	93	85	104
142	EL	2	N	41	F	1285017	173	1.73	75	25.1	I	2	>6.5cm	No	100	2a	14	73	73	72	70	70	65	74
143	EM	2	L	48	F	1296772	170	1.7	65	22.5	I	1	>6.5cm	No	90	2a	15	95	94	90	88	88	78	98
144	EN	1	S	68	M	1296727	170	1.7	68	23.5	I	2	>6.5cm	No	100	2a	14	94	90	89	85	84	80	94
145	EO	2	A	50	F	1297682	155	1.55	70	29.1	II	2	>6.5cm	Hypothyroid	100	2a	15	75	73	70	68	65	62	74
146	EP	0	N	24	M	408489	170	1.7	65	22.5	I	1	>6.5cm	No	100	1	14	91	92	90	88	90	85	108
147	EQ	2	S	72	F	1297866	155	1.55	70	29.1	II	2	>6.5cm	HTN	80	2a	15	88	85	85	84	84	75	90
148	ER	2	R	65	M	1332594	162	1.62	65	24.8	I	2	>6.5cm	No	100	2a	14	73	72	70	70	70	62	78
149	ES	2	S	62	M	1338657	165	1.65	60	22.0	I	2	>6.5cm	No	100	2a	14	80	78	75	75	75	70	84
150	ET	2	R	38	F	1311620	168	1.68	90	31.9	I	2	>6.5cm	No	100	2a	16	98	95	88	90	90	80	88
151	EU	2	A	57	F	1280526	157	1.57	65	26.4	I	2	>6.5cm	No	80	2a	15	88	85	84	80	80	75	90
152	EV	1	K	34	F	1309260	165	1.65	50	18.4	I	2	>6.5cm	No	100	2a	15	88	87	89	90	86	80	98
153	EW	0	BL	51	M	1302965	165	1.65	65	23.9	I	1	>6.5cm	No	120	1	14	68	68	67	69	70	65	79
154	EX	2	DJ	20	M	1302984	172	1.72	60	20.3	I	1	>6.5cm	No	140	1	15	93	95	94	90	98	98	88
155	EY	2	G	61	M	1329283	173	1.73	80	26.7	I	1	>6.5cm	No	120	2a	15	108	105	100	98	98	90	110
156	EZ	1	K	27	M	1329294	180	1.8	100	30.9	II	2	>6.5cm	Overweight	200	2b	15	82	82	80	78	78	70	105
157	FA	1	N	23	M	132950	180	1.8	90	27.8	I	2	>6.5cm	No	150	2a	16	65	65	64	63	64	60	74
158	FB	1	A	42	F	767936	165	1.65	70	25.7	I	2	>6.5cm	No	120	2a	16	94	90	90	88	85	80	95
159	FC	0	A	48	F	1327740	165	1.6	70	27.3	I	2	>6.5cm	NO	120	2a	15	84	85	84	80	82	75	99
160	FD	0	MK	37	F	202786	165	1.65	65	23.9	I	2	>6.5cm	No	100	2a	12	68	68	69	67	65	60	94
161	FE	2	M	40	F	1324374	157	1.57	65	26.4	I	1	>6.5cm	No	100	2a	15	86	84	85	84	85	75	84
162	FF	0	R	24	M	937123	162	1.6	70	27.3	I	1	>6.5cm	No	140	1	13	70	70	68	72	75	68	92
163	FG	1	M	46	F	1327412	165	1.65	65	23.9	I	2	>6.5cm	No	120	2a	15	94	90	90	88	85	78	96
164	FH	0	J	62	F	1326799	161	1.6	62	24.2	I	2	>6.5cm	No	140	2a	16	100	102	100	105	99	90	110
165	FI	1	VS	64	F	1304361	168	1.68	75	26.6	II	2	>6.5cm	HTN	130	2a	15	89	88	89	85	86	80	95

Serial No.	Study Code	Heart Rate_1 min	Heart Rate_2 min	Heart Rate_3 min	Heart Rate_4 min	Heart Rate_5 min	Heart Rate_6 min	Heart Rate_7 min	Heart Rate_8 min	Heart Rate_9 min	Heart Rate_10 min	SpO2_Before nebulisation	SpO2_During Nebulisation 5 min	SpO2_During Nebulisation 10 min	SpO2_After Nebulisation 5th min	SpO2_After Nebulisation 10th min	SpO2_Just before intubation	SpO2_Immediately after intubation	SpO2_1 min	SpO2_2 min	SpO2_3 min
127	DW	77	75	72	70	68	70	69	68	65	67	99	99	99	100	100	100	100	100	100	99
128	DX	77	75	72	75	73	74	70	72	72	70	99	99	99	99	98	99	98	99	99	99
129	DY	98	97	88	87	88	86	88	85	84	84	98	98	98	99	98	98	99	100	98	99
130	DZ	71	72	70	71	70	68	68	68	67	66	98	98	98	98	99	98	99	99	100	100
131	EA	98	98	96	95	90	88	87	88	85	83	98	99	99	99	98	99	100	100	100	100
132	EB	82	80	78	76	74	70	69	65	66	68	100	100	100	100	100	100	100	100	100	100
133	EC	70	70	71	68	65	65	63	60	62	59	96	97	98	99	98	98	99	99	99	99
134	ED	90	88	86	87	88	86	85	83	85	82	100	100	100	99	100	100	100	100	100	100
135	EE	76	73	73	74	73	71	70	69	68	72	100	100	100	100	100	100	100	100	100	100
136	EF	83	80	78	78	76	75	76	74	70	72	99	99	98	99	100	100	100	100	100	100
137	EG	93	90	89	88	89	90	88	87	85	83	98	99	99	99	99	100	100	99	99	100
138	EH	88	85	87	84	82	80	80	79	80	80	100	100	100	100	100	100	100	100	100	100
139	EI	95	96	94	90	88	89	88	85	84	80	100	100	100	100	100	100	100	100	100	100
140	EJ	98	95	95	93	92	90	88	89	88	86	100	100	100	100	100	100	100	100	100	100
141	EK	104	102	100	99	99	99	98	96	95	90	98	98	98	98	96	98	99	99	99	98
142	EL	70	69	68	69	67	67	68	65	64	64	100	100	100	100	100	100	100	100	100	100
143	EM	94	93	90	88	85	84	80	78	75	73	100	100	100	100	100	100	100	100	100	100
144	EN	92	90	89	88	88	85	84	83	84	80	98	98	97	98	99	98	97	98	99	98
145	EO	75	73	70	69	68	65	64	63	62	60	100	100	99	99	99	99	100	99	99	99
146	EP	107	110	105	100	98	96	94	92	90	90	100	98	99	99	98	99	99	99	99	100
147	EQ	90	88	85	84	82	81	82	80	78	78	99	99	100	100	100	100	99	99	100	100
148	ER	78	77	75	73	70	68	68	67	65	65	100	100	100	100	100	100	100	100	100	100
149	ES	80	78	77	78	75	74	73	72	74	70	99	99	99	100	99	99	99	99	99	99
150	ET	85	80	82	80	80	82	80	78	75	73	99	99	99	99	99	99	99	99	99	99
151	EU	90	88	85	84	80	78	75	70	68	70	100	100	100	100	100	100	100	100	100	100
152	EV	95	94	93	90	88	87	86	85	84	82	100	100	100	100	100	100	100	100	100	99
153	EW	78	79	75	74	72	70	70	69	65	64	100	100	100	100	100	100	100	100	100	100
154	EX	95	90	88	85	80	78	72	70	68	65	100	100	100	100	100	100	100	100	100	100
155	EY	108	105	100	102	103	100	98	95	93	90	100	100	100	100	100	100	100	100	100	100
156	EZ	104	100	101	98	95	93	90	89	88	85	99	99	98	98	99	99	99	99	99	99
157	FA	74	73	72	70	70	70	69	65	65	63	98	99	99	99	99	98	99	98	99	99
158	FB	94	90	88	85	84	83	82	80	80	79	99	99	99	99	99	99	100	99	99	99
159	FC	98	98	97	95	94	93	92	90	88	85	100	100	100	100	100	100	100	100	100	100
160	FD	92	92	90	88	85	80	80	75	79	70	99	99	99	98	99	99	98	99	99	99
161	FE	83	80	78	78	76	75	76	74	70	72	99	99	98	99	100	100	100	100	100	100
162	FF	90	90	88	85	84	82	80	78	75	73	99	99	99	99	99	100	99	99	99	99
163	FG	94	94	92	90	88	85	85	84	80	80	100	99	100	100	100	100	100	100	100	100
164	FH	110	108	105	108	105	100	98	95	90	88	99	99	100	99	99	99	98	99	99	99
165	FI	95	90	90	92	94	90	88	85	85	82	100	100	100	99	100	100	100	100	100	100

Serial No.	Study Code	SpO2_4 min	SpO2_5 min	SpO2_6 min	SpO2_7 min	SpO2_8 min	SpO2_9 min	SpO2_10 min	SBP_Before nebulisation	SBP_During Nebulisation 5 min	SBP_During Nebulisation 10 min	SBP_After Nebulisation 5th min	SBP_After Nebulisation 10th min	SBP_Just before intubation	SBP_Immediately after intubation	SBP_1 min	SBP_2 min	SBP_3 min	SBP_4 min	SBP_5 min	SBP_6 min	SBP_7 min	SBP_8 min	SBP_9 min	SBP_10 min
127	DW	100	99	100	100	99	100	100	125	124	120	125	126	110	128	125	120	118	118	116	114	116	118	120	110
128	DX	99	99	99	99	98	99	99	128	130	128	130	127	120	125	124	122	120	120	118	120	120	122	127	124
129	DY	98	99	98	99	99	98	99	117	115	115	115	112	99	140	138	120	132	128	125	127	126	126	125	120
130	DZ	100	100	100	100	100	100	100	128	130	130	128	122	118	125	125	121	125	123	120	118	118	117	120	114
131	EA	100	100	100	100	100	100	100	120	120	122	118	120	95	134	130	128	128	125	130	124	122	120	118	115
132	EB	100	100	100	100	100	100	100	118	115	120	116	115	98	140	138	135	134	130	132	128	131	125	120	118
133	EC	99	99	99	99	99	99	99	128	130	128	126	124	118	125	125	122	120	118	116	116	114	120	126	119
134	ED	100	100	100	100	100	100	100	130	128	130	129	125	105	128	125	123	122	120	118	115	114	116	112	110
135	EE	100	100	100	100	100	100	100	131	130	128	120	106	100	114	98	98	103	104	106	101	109	115	110	112
136	EF	100	100	100	100	100	100	100	122	120	124	120	125	98	120	118	110	112	111	115	114	108	110	110	105
137	EG	100	100	100	100	100	100	100	118	118	115	114	114	102	118	116	115	114	112	110	109	105	105	106	100
138	EH	100	100	100	100	100	100	100	127	128	125	124	122	118	130	128	130	126	125	120	118	115	116	117	112
139	EI	100	100	100	100	100	100	100	131	130	129	130	125	118	135	134	135	134	132	130	128	125	120	118	115
140	EJ	100	100	100	100	100	100	100	135	138	135	134	135	120	139	138	135	134	135	134	130	128	125	122	120
141	EK	99	99	99	98	99	99	99	125	125	130	128	125	110	135	134	135	134	130	125	120	120	118	118	115
142	EL	100	100	100	100	100	100	100	116	118	116	115	110	98	115	114	112	110	111	110	109	108	108	110	102
143	EM	100	100	100	100	100	100	100	117	115	114	115	110	100	125	120	124	120	118	114	116	114	110	113	110
144	EN	99	97	98	99	99	99	99	110	112	110	108	105	100	120	118	120	119	118	112	110	108	106	108	103
145	EO	99	99	99	99	99	99	99	126	125	124	120	118	115	125	124	122	120	118	116	115	114	112	112	108
146	EP	99	98	99	99	99	99	99	140	138	140	135	138	122	141	140	138	135	132	130	128	125	120	118	110
147	EQ	100	100	100	100	100	100	100	128	128	125	124	120	110	125	124	120	118	118	115	114	112	114	114	114
148	ER	100	100	100	100	100	100	100	116	116	110	108	105	98	120	118	118	116	115	112	110	108	108	107	99
149	ES	99	99	99	99	100	99	99	129	130	128	125	124	105	128	125	124	124	120	120	118	115	108	105	100
150	ET	99	99	99	99	99	99	99	116	115	114	112	110	98	116	114	110	116	115	114	112	110	112	112	99
151	EU	99	100	99	100	100	100	100	127	125	124	120	120	118	125	124	120	118	112	110	105	103	102	102	99
152	EV	99	100	100	100	100	100	100	132	132	135	140	135	120	140	138	135	132	130	128	125	124	122	120	118
153	EW	100	100	100	100	100	100	100	118	117	115	120	118	105	129	128	130	125	120	118	116	115	114	112	110
154	EX	99	100	99	100	100	100	100	120	120	118	110	112	98	110	108	106	105	104	107	105	102	100	100	95
155	EY	99	100	99	100	100	100	100	133	130	125	120	120	100	130	129	125	124	125	120	122	120	118	117	115
156	EZ	99	99	98	99	98	99	98	130	130	128	125	125	99	138	135	135	134	130	128	125	120	118	115	114
157	FA	99	99	100	99	99	99	100	140	138	135	130	130	118	142	140	138	135	134	130	128	125	126	120	120
158	FB	99	99	99	99	99	99	99	123	120	120	118	115	100	130	128	128	125	124	120	118	115	110	110	108
159	FC	100	100	100	100	100	100	100	115	115	114	116	118	100	130	130	128	125	124	120	118	118	115	112	110
160	FD	100	99	100	98	99	99	99	118	118	115	116	115	100	130	130	128	125	118	115	114	114	110	110	108
161	FE	99	100	99	100	100	100	100	122	120	124	120	125	98	120	118	110	112	111	115	114	108	110	110	105
162	FF	100	99	100	99	99	99	99	108	105	108	110	112	98	129	125	124	120	122	120	118	115	110	108	104
163	FG	100	100	100	100	100	100	100	125	124	120	120	118	102	128	128	125	120	122	120	118	115	110	110	108
164	FH	99	99	99	99	99	99	99	128	125	125	26	125	100	134	130	128	125	128	125	120	118	120	118	115
165	FI	100	100	100	100	100	100	100	140	138	135	135	134	125	144	140	140	138	135	135	132	130	130	129	125

Serial No.	Study Code	DBP_Before nebulisation	DBP_During Nebulisation 5 min	DBP_During Nebulisation 10 min	DBP_After Nebulisation 5th min	DBP_After Nebulisation 10th min	DBP_Just before intubation	DBP_Immediately after intubation	DBP_1 min	DBP_2 min	DBP_3 min	DBP_4 min	DBP_5 min	DBP_6 min	DBP_7 min	DBP_8 min	DBP_9 min	DBP_10 min	MAP_Before nebulisation
127	DW	60	60	58	52	54	48	60	60	58	56	52	52	53	55	48	52	50	82
128	DX	52	53	55	52	56	50	60	60	58	55	54	52	54	55	50	55	54	77
129	DY	72	72	70	68	70	60	90	76	75	80	71	78	75	77	75	74	75	87
130	DZ	87	87	85	80	80	65	80	75	81	78	70	70	74	72	68	64	75	101
131	EA	68	65	68	70	70	60	70	68	65	68	65	65	70	64	60	58	60	85
132	EB	60	58	60	64	60	56	88	86	84	80	78	80	78	70	68	64	62	79
133	EC	57	55	60	65	60	50	65	60	62	60	58	58	60	58	62	64	60	81
134	ED	68	70	65	68	65	60	68	68	66	63	58	58	60	62	58	58	65	89
135	EE	56	56	55	50	65	49	64	51	50	53	57	58	60	59	70	68	70	81
136	EF	75	73	76	72	78	65	75	74	72	70	70	68	65	70	65	68	65	91
137	EG	87	87	80	79	78	69	88	85	84	83	82	80	80	78	78	76	78	97
138	EH	76	76	75	75	70	65	80	79	79	75	74	70	68	65	63	60	60	93
139	EI	60	62	60	60	65	55	80	78	78	75	74	70	68	65	64	62	60	84
140	EJ	68	70	69	70	72	62	78	78	74	70	68	68	65	64	63	62	60	90
141	EK	88	89	90	85	84	68	90	90	92	90	88	86	80	78	75	74	70	100
142	EL	67	68	68	60	60	55	68	68	65	64	63	60	59	60	60	58	55	83
143	EM	87	82	80	80	68	60	80	79	80	78	78	78	70	70	68	65	60	97
144	EN	84	80	79	75	70	65	88	83	86	81	82	80	78	74	73	70	69	93
145	EO	77	75	74	70	68	60	68	65	64	62	60	58	55	53	50	50	52	93
146	EP	68	70	69	70	68	60	73	72	70	69	68	70	65	64	63	62	60	92
147	EQ	67	67	68	65	60	59	72	70	70	68	65	64	60	62	60	62	65	87
148	ER	76	72	70	69	65	60	80	78	75	74	73	70	70	68	65	65	62	89
149	ES	62	57	60	59	54	50	69	65	60	60	62	60	60	58	57	57	55	84
150	ET	67	67	68	65	65	60	72	70	68	65	63	63	65	68	64	65	60	83
151	EU	87	85	86	80	78	75	80	78	75	74	70	68	65	63	65	63	60	100
152	EV	75	78	78	78	75	70	78	76	76	73	68	70	69	68	63	64	63	94
153	EW	90	90	88	85	87	72	88	87	88	86	82	80	78	74	72	70	70	99
154	EX	89	87	78	76	74	62	78	75	74	72	72	70	70	71	70	69	68	99
155	EY	72	67	65	60	60	58	70	70	70	68	70	70	68	60	60	61	60	92
156	EZ	70	70	70	68	65	60	73	72	68	68	68	70	68	65	62	64	60	90
157	FA	70	70	69	65	65	58	68	68	68	66	63	65	65	64	61	60	60	93
158	FB	69	68	65	64	63	59	68	66	63	62	58	60	60	60	56	55	54	87
159	FC	75	76	75	78	75	60	70	72	70	68	65	65	64	60	60	58	55	88
160	FD	69	70	70	70	69	60	78	75	74	70	70	69	68	65	65	64	60	85
161	FE	75	73	76	72	78	65	75	74	72	70	70	68	65	70	65	68	65	91
162	FF	70	70	72	70	68	60	74	70	72	70	68	68	65	60	58	55	52	83
163	FG	83	85	85	82	80	70	83	86	78	76	73	70	70	69	63	64	60	97
164	FH	84	85	84	86	85	60	90	90	89	90	89	88	85	84	80	80	75	99
165	FI	90	88	85	82	80	65	93	90	88	83	82	82	80	80	76	78	75	107

Serial No.	Study Code	MAP_During Nebulisation 5 min	MAP_During Nebulisation 10 min	MAP_After Nebulisation 5th min	MAP_After Nebulisation 10th min	MAP_Just before intubation	MAP_Immediately after intubation	MAP_1 min	MAP_2 min	MAP_3 min	MAP_4 min	MAP_5 min	MAP_6 min	MAP_7 min	MAP_8 min	MAP_9 min	MAP_10 min	Adverse event	Treatment given
127	DW	81	79	76	78	69	83	82	79	77	74	73	73	75	71	75	70		
128	DX	79	79	78	80	73	82	81	79	77	76	74	76	77	74	79	77		
129	DY	86	85	84	84	73	107	97	90	97	90	94	92	93	92	91	90		
130	DZ	101	100	96	94	83	95	92	94	94	88	87	89	87	84	83	88		
131	EA	83	86	86	87	72	91	89	86	88	85	87	88	83	80	78	78		
132	EB	77	80	81	78	70	105	103	101	98	95	97	95	90	87	83	81		
133	EC	80	83	85	81	73	85	82	82	80	78	77	79	77	81	85	80		
134	ED	89	87	88	85	75	88	87	85	83	79	78	78	79	77	76	80		
135	EE	81	79	73	79	66	81	67	66	70	73	74	74	76	85	82	84		
136	EF	89	92	88	94	76	90	89	85	84	84	84	81	83	80	82	78		
137	EG	97	92	91	90	80	98	95	94	93	92	90	90	87	87	86	85		
138	EH	93	92	91	87	83	97	95	96	92	91	87	85	82	81	79	77		
139	EI	85	83	83	85	76	98	97	97	95	93	90	88	85	83	81	78		
140	EJ	93	91	91	93	81	98	98	94	91	90	90	87	85	84	82	80		
141	EK	101	103	99	98	82	105	105	106	105	102	99	93	92	89	89	85		
142	EL	85	84	78	77	69	84	83	81	79	79	77	76	76	76	75	71		
143	EM	93	91	92	82	73	95	93	95	92	91	90	85	85	82	81	77		
144	EN	91	89	86	82	77	99	95	97	94	94	91	89	85	84	83	80		
145	EO	92	91	87	85	78	87	85	83	81	79	77	75	73	71	71	71		
146	EP	93	93	92	91	81	96	95	93	91	89	90	86	84	82	81	77		
147	EQ	87	87	85	80	76	90	88	87	85	83	81	78	79	78	79	81		
148	ER	87	83	82	78	73	93	91	89	88	87	84	83	81	79	79	74		
149	ES	81	83	81	77	68	89	85	81	81	81	80	79	77	74	73	70		
150	ET	83	83	81	80	73	87	85	82	82	80	80	81	82	80	81	73		
151	EU	98	99	93	92	89	95	93	90	89	84	82	78	76	77	76	73		
152	EV	96	97	99	95	87	99	97	96	93	89	89	88	87	83	83	81		
153	EW	99	97	97	97	83	102	101	102	99	95	93	91	88	86	84	83		
154	EX	98	91	87	87	74	89	86	85	83	83	82	82	81	80	79	77		
155	EY	88	85	80	80	72	90	90	88	87	88	87	86	80	79	80	78		
156	EZ	90	89	87	85	73	95	93	90	90	89	89	87	83	81	81	78		
157	FA	93	91	87	87	78	93	92	91	89	87	87	86	84	83	80	80		
158	FB	85	83	82	80	73	89	87	85	83	80	80	79	78	74	73	72		
159	FC	89	88	91	89	73	90	91	89	87	85	83	82	79	78	76	73		
160	FD	86	85	85	84	73	95	93	92	88	86	84	83	81	80	79	76		
161	FE	89	92	88	94	76	90	89	85	84	84	84	81	83	80	82	78		
162	FF	82	84	83	83	73	92	88	89	87	86	85	83	78	75	73	69		
163	FG	98	97	95	93	81	98	100	94	91	89	87	86	84	79	79	76		
164	FH	98	98	66	98	73	105	103	102	102	102	100	97	95	93	93	88		
165	FI	105	102	100	98	85	110	107	105	101	100	100	97	97	94	95	92		

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No. BFUHS/2K21p-TH/ Date -/11/21

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Ashima Mahajan**, a student of your college for **MD Anaesthesiology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Role of pre-operative dexmedetomidine nebulisation 1 vs 2µg/kg in blunting haemodynamic response to larygoscopy and intubation.

Supervisor
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Co-Supervisor

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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any)

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

9. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
10. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2 µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

In

ANAESTHESIOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

March 2021

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ABSTRACT OF PLAN OF THESIS

Title	ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION
For the degree of	M.D. Anaesthesia
Name of the candidate	Dr. Ashima Mahajan
Supervisor	Dr. Suneet Kant Kathuria, Professor, Department of Anesthesia, DMCH, Ludhiana
Co-supervisor	Dr. Neeru Luthra, Associate Professor, Department of Anesthesia, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Dexmedetomidine, a potent, highly selective alpha-2 adrenergic receptor agonist have been used for blunting haemodynamic response to laryngoscopy and intubation through IV, intranasal and nebulised routes. Nebulised dexmedetomidine 1µg/kg effectively blunts increase in heart rate (HR) but not systolic blood pressure (SBP). Dexmedetomidine nebulisation with 2µg/kg dose may help in blunting both tachycardia and hypertensive response.

Aim of Study: Primary: Role of pre-operative dexmedetomidine nebulisation with 1 vs 2µg/kg in blunting haemodynamic response to laryngoscopy and intubation. **Secondary:** To compare propofol dose sparing & adverse effects associated with 1 & 2µg/kg nebulised dexmedetomidine.

Materials & Methods: A prospective, randomized, study will be conducted on 150 ASA I and II patients undergoing surgery under general anaesthesia with endotracheal tube (ETT) insertion, who will be divided into 3 groups of 50 patients each. In groups 0, I and II, patients will be nebulised for 10 minutes with 5 ml of 0.9% NaCl solution containing 0, 1 and 2 µg/kg dexmedetomidine respectively, 10 minutes before induction. Heart rate, Systolic, diastolic and mean arterial pressure (MAP) will be monitored and recorded at regular intervals and the data so collected will be analysed statistically.

Clinical Significance: To find the most effective dose of nebulised dexmedetomidine for blunting stress response to laryngoscopy and intubation with minimal incidence of complications.

Keywords: Laryngoscopy, Intubation, Nebulised Dexmedetomidine, Haemodynamic response.

(Signature)	(Signature)	(Signature)	(Signature)
Candidate	**Co-supervisor**	**Supervisor**	**Principal**

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION"** exist in the Department of Anaesthesiology at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
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Name of candidate	Dr Ashima Mahajan
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Topic of Thesis	ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION
Likely date of appearing in PG examination	MAY-JUNE 2023
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Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
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Approved: Yes / No

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Chairperson
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Approved: Yes / ~~No~~

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BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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3	COURSE OF STUDY AND SUBJECT	M.D. ANAESTHESIOLOGY
4	DATE OF ADMISSION OF COURSE	26th JULY 2020
5	TITLE OF THE TOPIC	ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Laryngoscopy and tracheal intubation generates pressure response in form of hypertension, tachycardia, increased intracranial and intraocular pressure and may be associated with myocardial ischaemia in susceptible individuals. These responses are thought to be somato-visceral reflex caused by stimulation of nasopharynx and laryngopharynx.[1]

Laryngoscopy alone can also generate essentially same pressor response as done by laryngoscopy followed by intubation. Although this response may be of short duration and of little importance in healthy individuals, but not so in patients with various co-morbid diseases such as coronary artery disease or intracranial disease.[2,3]So, it is important to blunt haemodynamic response to laryngoscopy and intubation, in order to keep patient in optimal condition during induction of anaesthesia.

Numerous drugs through various routes have been tried to attenuate stress response to laryngoscopy and intubation such as - opioids, beta-blockers, IV (intravenous) lignocaine but each of them have their own advantages and limitations.[4-7]

Dexmedetomidine is a highly potent, highly selective alpha-2 adrenergic receptor agonist. It has sedative, anxiolytic, analgesic and sympatholytic properties.[8-11]

Dexmedetomidine at an intravenous loading dose of 0.5 and 1µg/kg, attenuates increase in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP)[1] but IV bolus dose may lead to profound bradycardia and hypotension in cardio-compromised and hypovolemic patients.[4]

Intranasal administration of dexmedetomidine (1µg/kg) can also effectively alleviate stress response to tracheal intubation[12]. Disadvantage of intranasal administration is that, it can cause nasal irritation, cough, vocal cord irritation or laryngospasm.[4]

Nebulised dexmedetomidine 1µg/kg has been found to effectively blunt increase in heart rate, but not systolic blood pressure following

laryngoscopy and intubation.[5] In this study 1µg/kg of nebulised dexmedetomidine was evaluated and was unable to comment whether 2µg/kg dose will have better effect on haemodynamics. In order to find the most effective dose of nebulised dexmedetomidine to blunt stress response to laryngoscopy and intubation with minimal side effects, we plan to compare pre-operative nebulisation with 1 and 2µg/kg of dexmedetomidine.

6.2REVIEW OF LITERATURE

Laryngoscopy and intubation of the trachea is followed by sympathetic haemodynamic stress response that occurs as increase in DBP, SBP, HR and MAP [13,14]. This haemodynamic stress response to intubation is generally of brief duration and of little clinical significance in healthy individuals, but it is deleterious to those with systemic hypertension, coronary heart diseases, valvular cardiac diseases and the complications like hypertension, tachycardia, myocardial ischemia, left ventricular failure, cerebral haemorrhage and cardiac dysrhythmias can occur.[14-16] Many drugs have been used to blunt the cardiovascular response to laryngoscopy and intubation including lignocaine (intravenous and topical), magnesium sulphate and antihypertensive agents like phentolamine, sodium nitroprusside, beta blockers, nitroglycerine and calcium channel blockers [4-7]

Dexmedetomidine is a specific and selective alpha-2 adrenergic agonist. It has shorter duration of action and has sympatholytic, sedative, amnesic and analgesic properties.[8-11] It stimulates alpha-2 receptors in lateral reticular nucleus resulting in reduced central sympathetic outflow and blunting of haemodynamic responses to unpleasant stimulation and hence preventing the overall haemodynamic variability [17,18]. It produces co-operative or arousable sedation, which is different from clouding of consciousness induced by drugs acting on GABA system.

Dexmedetomidine as a IV bolus causes profound bradycardia and hypotension. Advantage of nebulised dexmedetomidine over intranasal is that, it avoids transient cough, nasal irritation, vocal cord irritation or laryngospasm.[19] Bioavailability of nebulised dexmedetomidine is 82% through buccal mucosa and 65% through nasal mucosa.[20,21]

M.-L. Jaakola et al.[22] conducted a study on 30 ASA I-II patients, for studying the effects of 0.6µg/kg of IV dexmedetomidine on intraocular pressure (IOP), haemodynamic and sympathoadrenal responses to laryngoscopy and intubation and on anaesthetic requirements in ophthalmic surgery. It was concluded that dexmedetomidine reduced IOP and attenuated the sympathoadrenal responses associated with

laryngoscopy and intubation. It also reduced the requirements for thiopentone, opioid and inhalation anaesthetic agents.

MuniseYildiz et al.[23] (2006) conducted a study on 50 patient divided into 2 group for studying effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation. It was concluded that pre-operative single dose(1µg/ml) of intravenous dexmedetomidine resulted in deep sedation, reduced opioid and anaesthetic requirements and blunted the haemodynamic responses following laryngoscopy.

Ola M. Zanaty et al.[19] (2015) conducted study on 60 children, aged 3-6 years, ASA I and II for comparison evaluation of nebulised dexmedetomidine, nebulised ketamine and their combination as premedication for outpatient pediatric dental surgery and concluded that a nebulised combination of low dose dexmedetomidine and ketamine produced more satisfactory sedation and provided more smooth induction of general anaesthesia, with more rapid recovery and no significant side effects.

MdShabazAlam et al.[2] (2017) conducted a study on comparison of effects of IV dexmedetomidine and IV magnesium sulphate on haemodynamic parameters in patients undergoing laryngoscopy and intubation. Studied was conducted on 100 patient divided into 2 groups. It was concluded that both drugs lead to haemodynamic stability.

Jose Luis Alvarez Juarez et al.[7] (2018) in a review article on adjuvant drugs to decrease the adrenergic response in conventional laryngoscopy, highlighted that there is great adrenergic and analgic discharge for patient undergoing tracheal intubation which can lead to serious complications, so adjuvant drugs like alpha 2 adrenergic agonist, magnesium sulphate, IV or local lignocaine can be used to decrease this stress response.

Neha Sharma et al.[24] (2018) conducted study on 90 ASA I and II patients for studying therapeutic efficacy of two different doses of dexmedetomidine on haemodynamic response to intubation and effect on induction dose of propofol. Patients were divided into three

groups.One group received 0.5µg/kg IVdexmedetomidine, second group received 1µg/kg IVdexmedetomidine and third group is control group. This study concluded that both doses were equally effective in blunting the haemodynamic responses to laryngoscopy and intubation and reducing the induction dose of propofol. A lower dose (0.5µg/kg) was associated with lesser incidence of adverse effects such as hypotension and bradycardia.

Danilo Nava et al.[1] (2018) conducted a study on 60 patients for evaluation of effect of IVdexmedetomidine on suppression of adrenergic response to laryngoscopy and intubation.1st group received dexmedetomidine dose of 0.5µg/kg and 2nd group received dose of 1µg/kg of same drug which was administered over 10 min, 10min before induction of anaesthesia. It was concluded that dexmedetomidine 0.5µg/kg intravenously causes hemodynamicstability pre and post-intubation with no adverse effects. Intravenous dose of dexmedetomidine 1µg/kg causes significant decrease in increased heart rate, SBP, DBP and MAP upto 3 min post-intubation.

Sana YasminHussain et al.[25] (2018) conducted a study on 90 ASA I and II patients, who were divided into 3 groups for evaluation and comparison of clonidine and dexmedetomidine for attenuation of haemodynamic response to laryngoscopy and intubation. Group C received2µg/kg of clonidine IV, group D received 1µg/kg of dexmedetomidine IV and group S received normal saline IV, infused over 10 minutes. It was concluded that attenuation of pressor response to intubation was better following premedication with the dexmedetomidine than with the clonidine.

XiaoxiaGu et al.[12] (2019) conducted a study on effect of intranasal dexmedetomidine as premedication on sedation and stress of tracheal intubation undergoing gynaecological laparoscopic surgery on 40 patients. Group A received 1ug/kg dexmedetomidine by intranasal route and Group B (control) received same volume of normal saline by intranasal route, 30 min before induction of anaesthesia. It was concluded that intranasal administration of dexmedetomidine (1µg/kg)

30 min before induction can alleviate stress response to tracheal intubation.

A study by SalkatNiyogi et al.[9] (2019) studied the comparison between intravenous (0.5µg/kg) and intranasal (1µg/kg) route of dexmedetomidine in attenuating haemodynamic response to laryngoscopy and intubation and concluded that both intravenous and intranasal route are equally effective for attenutation of haemodynamic stress response during laryngoscopy and intubation.

SatyajeetMisra et al[5]. (2019) conducted study on 120 ASA I and II patients, on effect of preoperative dexmedetomidine nebulisation on haemodynamic response to laryngoscopy and intubation and concluded that nebulised dexmedetomidine 1µg/kg attenuated increase in HR but not SBP following laryngoscopy and reduced the intraoperative anaesthetic and analgesic consumption. There was no effect on early postoperative nausea vomiting, sore-throat or increase incidence of adverse effects.

Nimmagadda R Kumar et al.[4] (2020) conducted a study on 100 ASAI,II patients, on evaluation of nebulised dexmedetomidine(1µg/kg) in blunting haemodynamic response to intubation and observed that, there was a dose sparing effect of propofol in group which received nebulised dexmedetomidine(1µg/kg) than control group. It was concluded that nebulised dexmedetomidine effectively blunts the stress response to laryngoscopy and intubation.In this study 1µg/kg dose of nebulised dexmedetomidine was evaluated and was unable to comment whether 2µg/kg dose will have better effect on haemodynamics. In order to find the most effective dose of nebulised dexmedetomidine to blunt stress response to laryngoscopy and intubation with minimal side effects, we plan to compare pre-operative nebulisation with 1 and 2µg/kg of dexmedetomidine.

6.3 AIMS AND OBJECTIVES OF THE STUDY

Primary aim:

- Role ofpre-operativedexmedetomidine nebulisation with 1 vs 2µg/kgin blunting haemodynamic response to laryngoscopy and intubation.

Secondary aim:

- To compare dose sparing effect of 1 and 2µg/kg dexmedetomidine nebulisation on propofol induction dose.
- To study adverse effects associated with 1 and 2µg/kg of dexmedetomidine nebulisation.

7. MATERIALS AND METHODS

7.1 SOURCE OF DATA

A randomized double blind observational study will be conducted in the department of Anaesthesiology, Dayanand Medical College & Hospital, Ludhiana after approval by Institutional Ethics Committee. A written informed consent will be obtained from each patient.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

- Age more than 18 years
- ASA I &II patients
- Patient with Mallampati class 1 or 2

EXCLUSION CRITERIA

- Pregnant females
- Patient with unstable haemodynamics
- Predicted airway difficulty
- ASA III & IV patients
- Known allergy to dexmedetomidine

GROUP ALLOCATION:

A total of 150 + 15 (to compensate dropouts) adult patients undergoing surgery under general anaesthesia with tracheal intubation will be included in this study.These patients will be allocated to either of 3 study groups of 50 + 5 (to compensate dropouts) patients each as follows:

GROUP 0 [control group] (n=50)

Patients will be nebulised for 10 minutes with 5 ml of solution containing 0.9% NaCl, 10 minutes before induction.

GROUP I: **(n=50)**

Patients will be nebulised for 10 minutes with 5 ml of solution containing 1µg/kg of dexmedetomidine in 0.9% NaCl, 10 minutes before induction.

GROUP II: (n=50)

Patients will be nebulised for 10 minutes with 5 ml of solution containing 2µg/kg of dexmedetomidine in 0.9% NaCl, 10 minutes before induction.

Randomization will be done by using computer generated random number list. Biostatistician, who will not be involved in further study will prepare coded, sequentially numbered and sealed envelopes, depending upon dose of nebulised dexmedetomidine.The allocated envelope will be opened by an anaesthesiologist who would not be involved with the direct clinical care of the patient and shall prepare the study drugnebulisationsolution as per random allocation sequence and label it with a code number and hand over study drug syringes to the anaesthesiologist for doing nebulisation and further case management. These codes would be decoded at the end of study period.

PREANAESTHETICCHECKUP

Routine thorough preanaestheticcheckup will be conducted comprising of detailed present and past history, comorbidities, history of allergy to any drug being used, general physical and systemic examination. Relevant investigations will be reviewed. Patients will be explained about the study being conducted and written informed consent will be taken.

ANAESTHESIA TECHNIQUE

On arrival in the operating room (OR), patients will be put on the operating table and routine monitoring in the form of 5-lead electrocardiography, non-invasive blood pressure (NIBP), temperature and pulse-oximeter and end tidal CO_2 ($EtCO_2$) will be instituted. IV access will be secured. Baseline HR, SpO_2, SBP, DBP and MAP will be recorded. Patients will be nebulised with study drugsolution over 10 minutes and haemodynamic parameters will be recorded at 5^{th} and 10^{th} minute of nebulisation. Post nebulisation haemodynamic parameters will be recorded at 5^{th} and 10^{th} minute.

10 minutes after completion ofnebulisation with dexmedetomidine, premedication in form of intravenous injection of midazolam 0.05mg/kg and metoclopramide 10mg will be administered. Patient will be pre-

oxygenated with 100% oxygen for 3-5 minutes with tight fitting appropriate sized face-mask. Anaesthesia will be induced with intravenous fentanyl 2µg/kg and titrated dose of 1% propofol intravenously till the patient's verbal response is abolished. Neuromuscular blockade will be achieved by usingatracurium 0.5mg/kg. Preintubation haemodynamic parameters recorded. After 150 seconds an experienced anaesthesiologist will perform laryngoscopy, and appropriately sized,styleted, endotracheal tube will be inserted in trachea, cuff inflated and connected to ventilator. After confirmation of correct placement and checking equal bilateral air entry, the endotracheal tube will be secured. Lungs will be mechanically ventilated using volume controlled ventilation using 35% oxygen in N_2O and 1.5% Isoflurane.

Haemodynamic parameters will be recorded immediately after intubation, and then after every 1minute for first 10 minutes. Fall in HR (<60bpm) will be treated with 0.6mg of IV atropine. Fall in blood pressure (SBP< 90mmHg) will be treated with incremental dose of 6mg IV bolus of ephedrine. Increase in BP and HRof more than 30% from baseline will be treated with 1 mg/kg IV dose of lignocaine and 30 mg boluses of IV propofol, repeated after every 5 minutes if needed. After 10 minutes of intubation or 2 minutes after return of BP and HR to baseline, whichever is later, the surgeon will be allowed to proceed for surgery and anaesthesiologist will be allowed to manage anaesthetic care of the patient during surgery as per institutional protocol. At end of procedure neuromuscular blockade will be reversed using IV injections of neostigmine 0.05mg/kg and glycopyrrolate 0.02mg/kg and ETT will be removed after confirming return of spontaneous and normal pattern of ventilation. Patient will be then be shifted to post-anaesthesia care unit for observation.

Outcome:

Primary outcome:

- To find most effective dose of nebulised dexmedetomidine with minimal side effect in blunting haemodynamic response to laryngoscopy and intubation by comparing HR, SBP, DBP and MAP

at pre-induction, pre-intubation,after-intubation and upto 10 minutes post intubation or 2 minutes after return of BP and HR to baseline, whichever is later.

Secondary Outcome:

- To compare effect of 1 & 2 µg/kg nebulised dexmedetomidineonreduction of induction dose of propofol.
- To compare incidence and magnitude of complication associated with use of 1 & 2 µg/kg nebulised dexmedetomidine.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using ANOVA. For comparing categorical data, Chi square (χ2) test will be performed and Fischer exact test will be used when the expected frequency would be less than 5. A probability value (p value)less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

SAMPLE SIZE CALCULATION

A post hoc power analysis was conducted using the software package, G*Power version 3.1.9.2 (Franz Faul, university kiel, Germany). The alpha level used for this analysis was $p<0.05$ and beta was 0.20. Sample size was estimated from the results of previous study[4]using MAP at 1 min as the parameter, which is the primary outcome of our study.Our sample size came out to be 50 subjects per group at power of 0.99 and with an effect size of 1.65 with 10% chance of error with $\alpha = 0.05$, $\beta = 0.20$ and confidence interval of 95%. Total cases 150.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached alongwith.

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DEPARTMENT OF ANAESTHESIOLOGY

DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA

PROFORMA

Serial Number: Date of surgery:

Study Code: Study Group:

Name: Age and Sex:

MRD Number:

DEMOGRAPHIC DATA

Height (cm): Weight (kg):

BMI (kg/m²): ASA grade:

Mallampatti Class: Thyromental distance:

COMORBIDITIES: _____

_____

Time of Nebulisation: _____

Time of Intubation: _____

Induction dose of Propofol: _____

Cormack- Lehane classification: _____

Time taken for intubation: _____

Signature of Candidate: _____ **Signature of Supervisor:** _____

HAEMODYNAMIC PARAMETERS

	Vitals	HR (bpm)	SpO_2 (%)	SBP mmHg	DBP mmHg	MAP mmHg	Adverse effect	Treatment given
During Nebulisation	Before nebulisation							
	5th minunte							
	10th min							
After nebulisation	5th minute							
	10th minute							
Intubation	Just before Intubation							
	Immediately after intubation							
After Intubation	1minute							
	2minute							
	3minute							
	4minute							
	5minute							
	6minute							
	7minute							
	8minute							
	9minute							
	10minute							

Signature of Candidate: _____ **Signature of Supervisor:** _____

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o..... .....am willing to participate in the study **"ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Supervisor **Signature of Candidate**

मरीज अनुमति फार्म

तिथि _____

मैं _____पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य **"ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____ਵਾਸੀ

_____

"ROLE OF PRE-OPERATIVE DEXMEDETOMIDINE NEBULISATION 1 VS 2µg/kg IN BLUNTING HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ